The American Journal of Surgery

is the leading independent surgical Journal. It publishes many papers read before the outstanding Surgical Societies, but it is *not* "the official organ" of any organization. Every manuscript is selected by the editors, as worthy of publication—nothing is published because "it was read at the meeting."

Copyright, 1936, by The American Journal of Surgery, Inc.

NEW SERIES, VOL. XXXIV DECEMBER, 1936 No. 3

EDITORIAL BOARD

Editor:

Thurston Scott Welton

New York

D. C. Balfour	*Rochester, Minn.*
Carl Beck	*Chicago*
Geo. R. Brighton	*New York*
Meredith F. Campbell	*New York*
James T. Case	*Chicago*
Isidore Cohn	*New Orleans*
Bradley L. Coley	*New York*
F. A. Coller	*Ann Arbor*
George W. Crile	*Cleveland*
E. C. Cutler	*Boston*
R. V. Day	*Los Angeles*
Charles A. Elsberg	*New York*
Herbert C. Fett	*Brooklyn*
C. R. G. Forrester	*Chicago*
H. Dawson Furniss	*New York*
J. H. Gibbon	*Philadelphia*
Emil Goetsch	*Brooklyn*
Charles A. Gordon	*Brooklyn*
Donald Guthrie	*Sayre, Pa.*
A. E. Hertzler	*Kansas City*
Louis J. Hirschman	*Detroit*
James M. Hitzrot	*New York*
Frederick C. Holden	*New York*
Emile F. Holman	*San Francisco*
J. A. Hyams	*New York*
R. H. Jackson	*Madison*
John E. Jennings	*Brooklyn*
W. L. Keller	*Washington, D.C.*
H. A. Kelly	*Baltimore*
T. J. Kirwin	*New York*
Arthur Krida	*New York*
A. V. S. Lambert	*New York*
Maurice Lenz	*New York*
H. H. M. Lyle	*New York*
Jerome M. Lynch	*New York*
Urban Maes	*New Orleans*
Harrison S. Martland	*Newark*
Rudolph Matas	*New Orleans*
Roy D. McClure	*Detroit*
H. C. Naffziger	*San Francisco*
C. R. O'Crowley	*Newark*
Louis E. Phaneuf	*Boston*
Eugene H. Poo	*New York*
Douglas Quick	*New York*
N. P. Rathbun	*Brooklyn*
H. A. Royster	*Raleigh*
Henry S. Ruth	*Philadelphia*
A. C. Scott	*Temple*
M. G. Seelig	*St. Louis*
J. Bentley Squier	*New York*
H. J. Stander	*New York*
George W Swift	*Seattle*
Grant E. Ward	*Baltimore*
J. H. Woolsey	*San Francisco*

EDITORIALS

THE CURRENT ISSUE OF THE AMERICAN JOURNAL OF SURGERY

IT is possible that greater interest is being manifested in anesthesia at the present time than during any preceding period following the first successful venture, almost a century ago, into the application of anesthetic drugs for the relief of the pain incurred by surgical procedures. This may probably be explained by several factors, the three most important of which have been the introduction of newer anesthetic agents and methods, the cooperation of a group of increasing numbers of surgeons, and the progress accomplished by medical men concentrating exclusively on anesthetic problems.

Of the new agents, it appears as though cyclopropane is the most important since it possesses characteristics common to no other gaseous inhalation anesthetic. Pentothal sodium and evipal are being employed at some institutions with increasing frequency. A few anesthetists have already placed great confidence in the technique of epidural anesthesia. The carbon dioxide absorption technique for the administration of inhalation anesthetics has proved to be of indispensable character. It is to be regretted, however, that in many instances, individuals will employ newly introduced agents with but little knowledge of their pharmacological action, their capabilities, their limitations and their dangers. Perhaps nothing is more detrimental to progress than persistent, ignorant and illogical application of the newer agents and methods.

The field of anesthesia is deeply indebted to the far-sighted surgeons and surgical staffs, who have realized the many virtues and indispensable character of an efficient department of anesthesia, composed of specialists in this subject. By cooperation and encouragement, both departments have profited. Conceptions of value concerning the importance and advocacy of possessing a medical anesthetic service can come only from those surgeons who have had

long contacts with this type of service. We are fortunate in being able to publish as editorials the ideas of three surgeons who perform their surgery under such conditions of anesthesia.

The present day possibilities of anesthesia have been accomplished largely by a number of anesthetists who have proved to be indefatigable seekers of improvement. They were dissatisfied with anesthesia which implies only obtundation of pain and provision of a suitable operative field. In addition, there was sought a maintenance of as near normal physiology during narcosis as is possible. They, therefore, attempted to provide for themselves and others, the necessary broad medical training in order to accomplish this. For it is now appreciated that a full knowledge of the basic sciences is essential to apply the older agents and methods more intelligently, and to derive the benefits and advantages offered by the newer portions of the available anesthetic armamentarium with safety. The efforts of these same anesthetists are responsible to a large extent for the formulation of some of the new techniques. Many laboratory investigators for a long time have been fascinated by the rich opportunities for research offered by the field of anesthesia. Close cooperation and association between those in research and those active in the clinical application of anesthesia have provided us with new agents and much valuable information. The activities of some anesthetists have emphasized the logic of placing the responsibility of resuscitation upon anesthetists. It was largely from these cited sources that the contents of this issue were obtained.

Henry S. Ruth.

Subscribers to The American Journal of Surgery *visiting New York City are invited to make the office of the publishers (The American Journal of Surgery, Inc., 49 West 45th Street, New York) their headquarters. Mail, packages or bundles may be addressed in our care. Hotel reservations will gladly be made for those advising us in advance; kindly notify us in detail as to requirements and prices.*

PROGRESS OF ANESTHESIA

THE field of anesthesia within the last few years exclusive of thoracic surgery, has perhaps shown greater progress and development than that of surgery itself. Surgical progress has been so remarkable that a large part of the slack, to speak figuratively, has been taken up. Surgical development continues but of necessity at a lessened rate of speed. Due to the fact that a large number of capable men have applied their minds so zealously to surgical research and surgical improvement, the field has been quite thoroughly worked.

Anesthesia within the last few years has been almost a virgin field with the result that development in it has been rapid, gratifying and almost startling. One of the factors which has restrained progress in anethesia has been the dominance of the surgeon over the anesthetist. It was the surgeon who selected the anesthetist and the anesthesia. He accepted also the responsibility for the anesthesia and not infrequently dominated its rate of induction and depth. Added to this situation is the fact that standardized ether anesthesia was, up to a few years ago and in many hospitals without trained anesthetists, perhaps wisely still is, the commonly employed anesthetic. Further add to this situation the fact that many anesthetists were inadequately compensated for their services and rarely saw the patients again after the operation and so attained little recognition and less satisfaction. Hence, one can readily appreciate the fact that there was little incentive for capable men to enter this field and to interest themselves in its development.

Fortunately, there is now growing up in this country an active group of anesthetists who by their organizing efforts are so raising the standards of anesthesia that they have won and earned for themselves and anesthesia the recognition which they deserve.

Hospitals will do well to acquire or have trained an anesthetist versed in the technique of the many new and varied types of anesthesia now available. The changing aspects in this field are evidenced by the fact that in the Lahey Clinic last year in 4232 anesthesias given, ether was used in only 389 cases and in only 142 of these was it the principal drug used. When one realizes that spinal anesthesia requires not only skillful introduction but much more important, most careful selection and even still more important, extremely careful watching for blood pressure and respiratory emergencies during its course, it becomes evident that the day when the surgeon can give spinal anesthesia for high abdominal operations and then turn the anesthesia over to a nurse for observation should be passing.

Some of the various types of anesthesia have but to be mentioned for one to appreciate their inestimable value to the patient and the surgeon; cervical block with metycaine in operations upon esophageal diverticulum, thus enabling the patients to swallow on request so that the sac can be readily identified; cyclopropane with its 50 to 85 per cent oxygen mixture for patients with severe hyperthyroidism, or with tuberculosis requiring thoracoplasty, or with primary carcinoma of the lungs and requiring removal of all of the lung on one side. In any case the patient rests upon the sound side of his chest and so is benefited by the high oxygen percentage in the anesthesia mixture; the value of intratracheal anesthesia in intrathoracic goitre, the indwelling tracheal catheter preventing collapse of the trachea and choking during the removal of the intrathoracic mass, the combination of intratracheal anesthesia, field block, and splanchnic anesthesia in the bad risk abdominal cases too handicapped for spinal anesthesia or ether; the employment of avertin anesthesia particu-

larly adapted for orthopedic cases and for nervous patients who can be put to sleep in their room and awaken again in their room; intravenous evipal anesthesia of a few minutes duration for removal of drains, the reduction of fractures and the manipulation of joints and sacral anesthesias for electrocoagulation of hypertrophied prostates.

The progress in anesthesia is distinctly real and practical. Trained anesthetists have much to offer the patient in the way of diminished discomfort and even more in the way of lessened risk. They have likewise much to offer surgeons in the way of making operating conditions easier for him. He will do well to seek and seriously consider their advice as to the type of anesthesia, the grade of risk and the need for emergency measures, transfusion or infusion during the operative procedure.

The newer forms of anesthesia demand capable and experienced men for their employment. Such men must not only be given recognition but the opportunity to train other men in this field.

The training of men in anesthesia has not kept pace with the other progress in this field. Hospitals will ultimately realize that the present attitude regarding relatively low cost anesthesia will prove a penny-wise and pound-foolish policy. Certainly one of the present practices in anesthesia should be frankly condemned; in the light of the present progress in anesthesia it is quite wrong for hospitals to show a profit by charging for nurse anesthetists, even though this profit is utilized in other departments of the hospitals. Nurse anesthetists definitely have their place under physician anesthetists in keeping hospital costs down but not as income earners for hospitals. If there should be a surplus income for anesthesia, it should be devoted to that for what it is paid by the patient, that is the best anesthesia possible and the training of better anesthetists.

Frank H. Lahey.

ANESTHESIA IN THE MEDICAL SCHOOLS

LET us hope that this issue is evidence of a Renaissance in anesthesia.

Introduced in America ninety years ago, enthusiastically received throughout the world, and impelled by the ever increasing needs and opportunities for its application, one would have predicted that the development of this specialty would have been systematic, logical and continuous. Contrary to this expectation its progress has been apathetic. For this apathy the medical school has been chiefly responsible, the surgeon particularly and the anesthetists specifically.

In medical education the notion has prevailed that if anesthesia were taught it could be presented by any lecturer, regardless of training and special scientific background. Its importance was minimized; its interest depreciated. Graduates in medicine who, by choice, or not rarely for reasons less worthy of admiration, became specialists in anesthesia, did so by the simple convenient method of self proclamation. Their education was obtained through experience and by the slow, dangerous process of trial and error. They had no opportunities to learn from the masters in the science. Thought, study and action were undisciplined.

It has long been recognized that cooperation between the different branches of science is essential to progress. Most of the advances in medicine have resulted from the reflection of new knowledge in one science upon the problems of another. Modern surgery is composed of an extraordinary large number of intricately related factors, not the least important of which is anesthesia. Surgery has neglected its handmaiden and become absorbed in technique. The ultimate goal, anesthesia which offers the utmost in convenience and does not expose the patient to serious dangers, cannot be obtained without the cooperation of surgery, anesthesia and its allied sciences. Changes and experiments must come and future advances must be made with confidence and promise. The surgeon must walk arm in arm with the anesthetist along this road of clinical efficiency.

The aspirant in anesthesia should be given encouragement and opportunity—two requisites which at present are insufficient. This is medical education and it should be developed in medical colleges and affiliated institutions. The leaderships should be placed in the hands of men versed in theory and possessing critical ability, originality and developed judgment. Under university regime, a rigid scientific spirit may be directed toward practical problems and the study of these problems encouraged under the best conditions. Recently, in a surprisingly few isolated instances, such organizations have been developed. The need to increase this number is acute. It is determinate upon Surgery to accept this responsibility and further the progress of its most essential accessory or suffer the consequences of inaction.

ARTHUR M. WRIGHT.

ANESTHESIA AND SURGERY

SINCE time immemorial means to alleviate pain and suffering have been sought. The great stumbling block to advances in surgery was the absence of a suitable agent. With the advent of the nineteenth century and the discovery of oxygen and nitrous oxide, the anesthetic possibilities of nitrous oxide were recognized by Sir Humphrey Davy. Valerius Cordis had discovered ether in the sixteenth century and recognized its power to allay pain. Both of these agents had to wait until their clinical possibilities were discovered. Ether had to wait for Long and Morton. It was fortunate indeed that this new agent was a 100 per cent anesthesia, for its application was universal and the margin of safety great enough so that a novice could give it; and it was given to the novice to administer and has remained there. Advances in anesthesia were thus held up because anesthesia, together with antisepsis and asepsis, opened up new fields—not only in surgery but in all branches of medicine. The advances that have been made resemble some of the medieval periods, in that it was due to individuals who might happen to be interested in some new drug and its pharmacologic action. Such men as Koller, Corning, Schleich, Crile and Luckhardt have contributed to the discovery of cocaine as a local agent, the hypodermic and spinal anesthesia, infiltration anesthesia, anoci-association and ethylene. Within recent years, due to a new interest in anesthesia on the part of the medical profession, investigation has revealed many new facts. These facts have been applied clinically so that anesthesia presents a much wider field.

The clinical application, for the most part, was effected through the clinical efforts of the surgeons who were interested in the subject of anesthesia. Within the present generation there has arisen an interest in the science and art of anesthesia in medical men who are not primarily surgeons. Due to their efforts the science of anesthesia has progressed and the art has been greatly amplified.

Anesthetic agents have been classified depending on the depth of anesthesia that can be produced. There are only five 100 per cent anesthesia agents: ether, chloroform, ethyl chloride, vinyl oxide and cyclopropane. The other agents used in anesthesia are only capable of reaching up to and into the third stage.

The difference patients present to the taking of an anesthesia depends on their metabolism. The metabolism represents the reflex irritability of the patient and the oxygen need. The metabolic condition of the patient and the type of operative interference planned determine the preoperative medication and the anesthetic agent that is to be used. The metabolic rate is influenced by age, endocrine imbalance, fever, pain and emotional excitement.

Anoxemia, acapnia, hyperpnea, acidosis and alkalosis play a role in each anesthetic. With the newer anesthetic agents where the limits of safety are narrower, and the change from one stage to another occurs very rapidly, the science of anesthesia is very closely related to the art.

The stages of anesthesia have been divided into four. The third stage has four planes. The amount of anesthesia necessary to allay reflex excitability of different tissues has been determined. Anoxemia, acapnea and hyperpnea have been evaluated as to the physiologic results on tissue. The potency of anesthetic agents with reference to the stage of anesthesia that may be produced has been determined. A rational basis for premedication of operative cases has been formulated. New methods of application of anesthetic agents have been worked out and new signs for the different depths of anesthesia discovered. These facts with their clinical application present a much greater field, and in order to master them necessitates a special preparation in this field conferable to any field in medicine. A general medical training is necessary, and also a special study of the basic sciences with reference to anesthetic agents, and also a skill in the art.

ERWIN R. SCHMIDT.

THE RECOGNITION OF ANESTHESIA AS A SPECIALTY

ANESTHESIA, as a practical aid to surgery, was born and fostered in the United States and while many physicians have been accepted by both the lay and medical public as specialists in this branch of medicine, the art itself has not been recognized officially by our national governing body, although most foreign medical associations and some of our own state medical societies have done so and granted sections on anesthesia.

If this oversight is intentional and based on standards maintained two or three decades ago, there might possibly be some excuse for this omission but today's progress in anesthesia, evidenced by marked advancement in the technique of administration, evaluation of the risk to patients, new agents and apparatus, analyses of end results and research findings, and improved methods of detailed instruction, entitle physicians practicing this art to the same consideration and prestige that recognition bestows upon practitioners of other medical endeavors.

These advancements are the result of the activities of national, international and local anesthesia societies aided by pharmacologists, physiologists, surgeons, biochemists, cardiologists and inhalation therapeutists together with the papers and demonstrations offered by the members at the stated meetings.

Excellent journals devoted to anesthesia and its corollary subjects are published regularly and books written by the individual members are available to the students, graduates and undergraduates in most medical libraries. Regular services are now open and often compulsory for internes involving definite curricula and instruction and three or four schools for postgraduates are functioning.

These schools require from one to three years attendance for the full course during which time the students are taught clinically and didactically all that pertains directly or remotely to anesthesia, (local, regional and general), analgesia and nerve block for pain relief.

Recently a university here has granted an M.S. and a PH.D. in Anesthesia to graduates of one of these schools, while other graduates are in demand by progressive hospital and medical schools who are rapidly establishing professorships in this specialty.

Certification of qualification is now an actuality by the Associated Anesthetists of the United States and Canada while the American Society of Anesthetists have granted Fellowships to over one hundred physicians representing some twenty-eight states in the Union. To be eligible for this Fellowship the physician must present indisputable evidence of qualification and meet the high standards which are on a plane with those demanded by other specialty boards.

The modern anesthetist worthy of the term is no longer satisfied with just a knowledge of the physiological action of anesthetic agents and a certain skill in their administration but feels that it is essential for him to have a working conception of neuroanatomy for spinal and other nerve blocks, physiology of respiration and circulation, pharmacology, biochemistry, the interchange of gases, electrocardiology, oxygen metabolism, inhalation therapy, endotracheal and endobroncheal intubations and resuscitation, including cardiac massage and cardiopuncture, together with physical diagnosis.

With the exactions of modern surgery, especially the advances in thoracic and brain operations, it may be necessary for the anesthetist to call upon any or all of this knowledge in order that the surgeon may operate in comfort and the patient assured the maximum safety.

Have other specialties done any differently?

T. DRYSDALE BUCHANAN.

PREOPERATIVE ESTIMATION OF THE ANESTHETIC AND SURGICAL RISK*

P. D. WOODBRIDGE, M.D.

Anesthetist, New England Deaconess and New England Baptist Hospitals

BOSTON, MASS.

POSTOPERATIVE morbidity and mortality may be reduced if the adverse factors which each patient presents are duly evaluated and heeded. Diligent search for these factors is rarely necessary—they are present as red flags in the usual history, physical examination and laboratory data, but the surgical train may rush the patient heedlessly past them toward the goal of operation with occasional unnecessary disaster. Due appreciation of the hazards presented by the patient's condition will affect choice of anesthesia (treated in this issue by L. F. Sise), choice of operation, preparedness for untoward events during and after operation, and most of all, the preoperative treatment employed, and by these means will favorably influence the outcome. "Careful preparation of the patient . . . often turn[s] a very poor risk into a fair or good one and save[s] days or weeks . . . in the subsequent convalescence, . . . if not life itself" (Wells[35]).

SCALES FOR GRADING RISKS

It is a distinct safeguard if each physician who goes over a case will note on the record his estimation of the degree of risk presented by the patient. A surgeon would hesitate to choose the more dangerous of two available operations in the face of written warnings from his internist, his anesthetist and his assistant. The International Anesthesia Research Society presents a very commonly used scale of A, B, C defined thus: "A: The good risks: patients free from organic disease, whose surgical condition is not likely to prove fatal. B: The fair risks: patients suffering from organic disease but whose surgical condition is not especially serious. C: The poor risks: patients whose surgical condition is so serious or so far advanced as likely to result in fatality." This scale provides no suitable classification for patients with extremely severe "organic disease" and mild "surgical condition." Some who have used it have found it inadequate, and have added a confusing array of other letters. We have found it more satisfactory to employ the scale ordinarily used for rating signs and symptoms (1, 2, 3, 4, meaning respectively slight, moderate, marked, and extreme). Thus "1" means Good Risk: nothing found in the patient's condition that adversely affects the risk; "2" means Fair Risk: one or more adverse factors are present, but are not serious; "3" means Poor Risk: prepare patient carefully for operation, choose the least operation that will give the needed surgical relief, and select the anesthetic drug and method with special regard to the patient's condition—this is, therefore, an unmistakable danger signal; "4" means: so seriously sick that death is likely unless the downward progress is quickly reversed. For this classification all unfavorable diseases and conditions the patient presents, whether "medical" or "surgical," are considered together, including the condition for which operation is to be performed. The severity of the proposed operation is not taken into account. Thus if a patient has severe hyperthyroidism, that alone marks him as a grade 3 risk, whether the operation proposed is thyroidectomy or merely reduction of fracture of a phalanx. In this way serious misunderstandings are

* From the Department of Anesthesia, Lahey Clinic, Boston, Mass.

avoided which might arise if the proposed operation were taken into account, for the operation might be changed at a moment's notice.

GENERAL FEATURES

In most cases more important information will be gotten from a few minutes of inspection of, and of talk with the patient, and from the hemoglobin estimation and the urinalysis, than will be found in all of the rest of the physical examination or laboratory data. The points of prime importance to be gleaned from such a brief interview are considered in this section and in the two that follow.

Age. An age of 55 years or over almost automatically takes the patient out of the grade 1 group. Butler, Feeney and Levine[2] found three times as many operative deaths in patients with heart disease over fifty years as in those under fifty years, and Miller[20] in an unselected series of general surgical cases found eight times as many deaths in those over fifty years.

Weakness. The usual laboratory reports throw no light on weakness and debility, and mention of them is too often omitted from records of physical examinations, yet they are of *the utmost importance.* The evidence comes from questioning and observing the patient, and from questioning the attending nurses. Moderate and severe degrees of weakness automatically brand patients as fair and poor "risks" respectively. *Prolonged invalidism* is of equal importance.[5]

Psychic State. A much depressed psychic state augurs ill for the period of convalescence. It is well to take heed of a definite *premonition of death.* In order to prevent the fulfilment of a powerful autosuggestion of this sort, it may be well to "steal" upon a patient so afflicted with a rectal anesthetic under the guise of giving a cleansing or nutritive enema, or with an intravenous drug under the guise of taking a blood sample.

Changes in Weight. Marked *obesity* presents a moderate though definite handicap.[5,34] It interferes with breathing whether the patient is under spinal or general anesthesia; it increases the difficulty and therefore also the trauma of abdominal operations; and it appears to make the patient more prone to develop complications during convalescence. On the other hand, more than a slight pathological *loss of weight* carries with it a parallel increase in the operative risk involved, probably due in large part to the depletion of glycogen reserve with resultant partial starvation of body tissues generally. In a series of 50 patients operated on for peptic ulcer, Studley[30] found a mortality rate of 33⅓ per cent in those who had lost 20 per cent or more of their body weight, as contrasted to a rate of 3.5 per cent among those who had lost less weight.

Vomiting. Persistent vomiting may plunge the patient very rapidly into an extremely grave condition because of the resulting acute starvation and acidosis. Ketonuria, a lowering of the carbon dioxide combining power of the blood, and sometimes a lowering of the *p*H value of the blood are corroborative data (Thalhimer[33]) The gravity of the risk may be lessened by the intravenous administration of glucose. Some prefer to give insulin with the glucose, since it helps not only in oxidizing glucose and thus in overcoming the acidosis, but also aids in storing glycogen.

High *intestinal obstruction,* on the other hand, produces degrees of alkalosis fully as serious as the acidosis of simple starvation. The chlorides of the blood are reduced and its content of nonprotein nitrogen is elevated. The risk should be lessened before operation is undertaken by the intravenous administration of physiological solution of sodium chloride.[33]

OXYGEN METABOLISM

It is likely that a basic function of most anesthetics is to interfere with cellular oxidation. Moreover several of the inhalation agents, as commonly given, tend to displace oxygen in the respiratory tract, while rectal, intravenous and spinal anes-

thesia frequently diminish the tidal respiratory volume to the point of producing varying degrees of anoxemia. Anoxia, or oxygen starvation of the tissues, is therefore an eternal problem to the anesthetist, and any additional pathological block to the free passage of oxygen to the tissues is of utmost importance in establishing the anesthetic risk, whether the block be mechanical, or chemical as from toxins.

Any mechanical *obstruction to free breathing*, such as ankylosis of the jaw, nasal blocking, an abscess bulging into the pharynx, paralysis of a vocal cord, or compression of the trachea from a mediastinal tumor, presents an important problem to the anesthetist which must be met by careful choice of anesthetic method and drug (such as cyclopropane with large proportion of oxygen, the intratracheal method, or the auxiliary use of helium), or rarely by preliminary tracheostomy.

Diminution of the *vital capacity* to less than half of the normal, definitely increases the anesthetic risk. Vital capacity varies directly with cardiac efficiency[16,23] and is lessened by emphysema, pulmonary tuberculosis, and other inflammations of the lung parenchyma and of the pleura. Pneumonias that accompany gas poisoning, measles and influenza are sometimes followed by fibrosis rather than by resolution, with resulting marked reduction of alveolar wall area and consequent increase of hazard in the use of drugs administered with low concentration of oxygen, such as nitrous oxide.[13] Percussion and auscultation in these cases give deceivingly negative findings. "The closer the vital capacity approximates tidal air, the graver the risk" (Moersch[21]).

The most frequent block to oxygen transportation is in the blood itself. The laboratory datum that most often serves as a danger signal to the anesthetist is the hemoglobin determination. It is not commonly realized that even as little as a half hour's administration of the usual inhalation anesthetics produces a significant reduction in the oxygen-carrying power of the blood, quite in addition to alterations in erythrocyte count and hemoglobin content.[32] "It seems to me nothing short of criminal to perform a major operation on a patient whose hemoglobin is lower than 70 without first alleviating the *anemia* with transfusions" (Thalhimer[33]). With the general tenor of this statement I would agree, but would qualify it by stating that many cases may well be handled by transfusion immediately following operation. We have found it safer to transfuse several hours or a day before operation rather than immediately beforehand. *The importance of anemia in determining anesthetic risk cannot be overestimated.*

CARDIOVASCULAR SYSTEM

Well over half of the recent literature on anesthetic risk deals with the heart and blood vessels. This great overemphasis is probably due to mistaking the cardiovascular signs of death for the primary cause of death. "Heart failure" is written on many death certificates that might better read "Surgical shock," "Postoperative obstruction of bowel," "Hemorrhage," "Asphyxia from respiratory obstruction," or "Poisoning from overdose of anesthetic agent." Butler, Feeney and Levine,[2] in an excellent analysis of convalescence from 494 operations on patients with definite heart disease, conclude that in the absence of nephritis or of a history of congestive failure or of coronary thrombosis, heart disease has little effect, if any, on operative mortality. Concerning another series of 336 operations on patients with heart disease, Hickman, Livingstone and Davies[8] conclude that as a group they are "fairly good risks."

To determine the degree of risk involved, various *mathematical indexes* based on the blood pressure and the pulse rate have been widely used. Some[27] place considerable faith in them, but most find them very unreliable.[4,14,31] Sykes very suitably ridicules them by reporting 8 cases in which the indexes gradually changed from "Bad risk—inoperable" to "Good risk—oper-

able" as each patient approached death from apoplexy, carcinoma, heart disease, phthisis, duodenal ulcer, or influenza. "Moot's rule"* is so figured that it would classify a large proportion of patients with severe hyperthyroidism as inoperable; and the "Energy Index"† would designate many patients in severe shock as "good risks." When normal, they appear to be of little or no value; when abnormal, they may be helpful by corroborating other more important data. The *breath-holding test* of Sebrasez is probably more significant,[6,27,29,34] but due allowance must be made for the individual's will power, training (chiefly of swimmers), and degree of intelligent cooperation. While resting in bed, the patient closes his mouth at the end of a deep inspiration, pinches his nose, and holds his breath as long as he can. A result of twenty-five seconds or more is normal, and one of fifteen seconds or less is held to indicate marked reduction of cardiac or respiratory reserve. A normal result in patients with heart disease is significant.[27]

The most important information concerning the heart and circulation is to be obtained by briefly questioning the patient concerning dyspnea and chest pain. "A *history* of the patient's activities and symptoms is far more valuable than the physical examination. . . . If the individual is able to indulge in moderate activity without symptoms, no concern need be felt about the ability of the heart to sustain the very slight extra work entailed by a surgical operation provided the anesthetic is properly administered" (Marvin). Rodman and Leaman[25] speak of "the folly of basing any opinion upon what is heard over the heart by the use of the stethoscope; for the purpose of operation and anesthesia, a heart which carries its daily burden well, without excessive dyspnea or chest pain, is equivalent to the normal organ." Sir James Mackenzie contrasted symptoms with mechanical tests thus:

> The standard by which the heart's strength is to be measured is not . . . fixed. . . . The field of normal response to effort varies widely in different healthy individuals. . . . The amount of effort he can normally put forth without distress . . . is the only practical standard by comparison with which it can be determined whether the field of the heart's response to effort is restricted. The subjective symptoms of heart failure are *never* absent when the heart's efficiency is in any way impaired.

In the early stages of heart failure "the patient becomes conscious of certain sensations of distress or discomfort on making an effort which formerly he was able to make without experiencing these sensations."

A simple and most valuable outline for *cardiovascular examination and grading*, parallel to those of the American Heart Association, is presented by Rodman and Leaman,[25] and could be adopted advantageously by everyone in rating cardiac patients for operation:

> "Class 1. Good risk. [This corresponds to our anesthetic risks 1 and 2.] Patients in whom ordinary physical activity does not cause undue fatigue, palpitation, dyspnea, or chest pain. All cases of well compensated valvular heart disease except the syphilitic; hypertensive heart disease with no renal involvement.
>
> "Class 2. Risk fair with careful medical supervision and preoperative treatment. [This corresponds to our anesthetic risk 3.] Emergency surgery only until risk improves. Cases of beginning congestive failure and angina. These all show undue fatigue, palpitation, dyspnea, or chest pain on *ordinary* physical activity. All patients classed here can have risk improved to class 1, if operation is not emergency.
>
> "Class 3. Surgery contraindicated. [This corresponds to our anesthetic risks 3+ and 4.] These patients show signs of cardiac insufficiency at rest, or signs of active heart infection. They cannot carry on *any* physical activity

* Pulse pressure in mm. Hg divided by diastolic pressure; 40 per cent to 60 per cent is called "operable"; below 25 per cent and above 75 per cent is called "probably inoperable."

† The value of the systolic pressure in mm. Hg is added to that of the diastolic pressure, and the sum is multiplied by the number of heart beats per minute. From 12,000 to 18,000 is considered normal.

without discomfort. Here we include severe angina patients, cases of cardiac decompensation with edema and severe dyspnea, and patients with recent coronary occlusion with marked reduction of the myocardial reserve."

Concerning the importance of various *lesions* and conditions, it is generally agreed[2,7,8,9,15,24,25] that coronary occlusion, angina pectoris, congestive failure and syphilitic aortitis carry high operative mortality; and that valvular heart disease and auricular fibrillation if uncomplicated by failure, and paroxysmal auricular flutter, fibrillation, or tachycardia do not add appreciably to the anesthetic or surgical risk. The risk attending congestive failure may be greatly lessened by preparation with digitalis and rest. Pulsus alternans, heart block, and bundle branch block (producing reduplication of the first sound at the apex) are regarded as very serious by some, but it is probable that their importance varies directly with the severity of symptoms of the diminished cardiac efficiency which may accompany them.

High blood pressure, even in the extreme range, if unaccompanied by myocardial or renal insufficiency, diabetes, hyperthyroidism or the like, adds only slightly to the operative risk (McQuiston and Allen[19]). This is probably contrary to the popular view, but is corroborated by others (Butler, Feeney and Levine,[2] Hermann[7] and Hickman, Livingstone and Davies[8]). Marked degrees of arteriosclerosis increase the risk slightly and require careful choice of anesthetic drug and method.

McQuiston also analyzed 250 cases of *low blood pressure*[18] uncomplicated by jaundice, diabetes, syphilis or Addison's disease, and found the mortality rate lower than in a parallel group with normal pressure. His series consisted of 100 cholecystectomies, 100 operations on stomach and duodenum and 50 gynecologic operations on patients whose systolic pressure was not higher than 100 mm. Hg. Life insurance statistics have shown the mortality rates among persons with low pressures to be but 35 per cent of the expected rates.

If a patient's usual pressure has been lowered by disease or other pathological state such as *shock*, the risk is increased proportionately to the amount of lowering of the pressure.

HEPATIC INSUFFICIENCY

Knowledge of the normal and abnormal functioning of the liver is woefully crude and fragmentary. Its relationship to anesthesia is probably supremely important because of its detoxifying power, its metabolizing of carbohydrates and storing of glycogen, and the injury which anoxemia and some anesthetics inflict upon it. No test or tests of its function have received even general approbation and common application.

Risk of hepatic failure may be minimized by the administration of liberal amounts of carbohydrate before operation.[10] In cases of suspected liver damage, such as may occur from prolonged sepsis, toxicity or starvation, the supply of carbohydrate should be even more bountiful in order to build up the glycogen reserve. This is important for detoxification, repair of liver damage and reduction of clotting time.

Obstructive jaundice is likely to be followed by postoperative hemorrhage.[10] The risk is therefore serious. No reliable prediction of the likelihood or severity of bleeding may be made from consideration of the degree or duration of jaundice or from the bleeding and clotting times as ordinarily performed. However, in about 30 of our cases in which the bleeding time has been obtained according to the method of Ivy,[11] it has predicted correctly the probability of hemorrhage. Transfusions, carbohydrates, and calcium gluconate are used to reduce the bleeding time (Ivy) and the likelihood of hemorrhage.

In the presence of hepatic insufficiency, anesthetic agents should be chosen which have the least toxic effect on the liver and which do not depend on the liver for detoxification.

DIABETES

Since the advent of insulin, Joslin[12] and others[1,17] have been preaching that diabetes, if properly treated, does not influence the surgical risk materially. According to our scale of grading, the untreated diabetic would fall into grade 2, 3 or 4, depending on the severity of the disease, and with suitable treatment he would be raised to grade 2 if there were no additional unfavorable factors. It is to be remembered, however, that if diabetes is of more than five years' duration, arteriosclerosis is probably present, and that if gallstones or gangrene are present, there is almost surely coronary disease also (Joslin[12]).

"Glycogen in the liver is everything to the diabetic. With it, his life is secure; without it, he dies," (Joslin[12]). He should therefore receive an adequate diet including adequate carbohydrate for glycogen storage, and sufficient insulin to keep the urine free of sugar and if possible to hold the blood sugar below 0.150 per cent (Allan[1]). "Give him carbohydrate within three hours of his operation: orange juice, strained cereal, ginger ale. Give too little insulin rather than too much" (Joslin), in order to avoid a hypoglycemic insulin reaction. In case the surgical disease involves acute infection, operation should be performed immediately without waiting for the usual preoperative treatment of the diabetes. That will be less severe when the burden of the surgical disease has been removed. The lifting of the load of hyperthyroidism or of gallstones by operation likewise ameliorates diabetes (Joslin[12]).

Severe acidosis with threatening coma involves the most serious risk. Tests for urinary acetone and diacetic acid are positive; the breath smells of acetone; estimation of the carbon dioxide combining power of the blood gives corroborative evidence. The risk should be lessened by vigorous treatment with carbohydrates, insulin and fluids. After acidosis has been overcome, the patient should be kept on an adequate carbohydrate diet (at least 50 to 100 gm. daily), with insulin if needed, free of ketonuria and of glycosuria, for several days before operation in order to allow the heart to recover from the injury inflicted on it by the state of acidosis. This recovery is indicated by the gradual drop of the pulse rate toward normal.[28]

RENAL INSUFFICIENCY

Certain anesthetics impair kidney function, others depend largely on the kidneys for their passage from the body, and operation throws a heavy additional load on the kidneys by reducing the available fluid through perspiration, hemorrhage, vomiting, diminution of fluid intake and shock, as well as by increasing the nitrogenous waste products in the blood through protein destruction associated with fever and operative trauma.[3] Any impairment of renal function increases the risk of anesthesia and of operation in corresponding degree.

In the presence of hypertension, general arteriosclerosis or albumin and casts in the urine, one or more tests of renal function should be done. The kidneys should be able to concentrate the urine to a specific gravity of at least 1.024,[3] the fractional phenolsulphonphthalein test should normally show excretion of 55 per cent in the first half hour,[26] and the nonprotein nitrogen of the blood should not exceed 40 mg. per hundred c.c. Blood urea nitrogen of over 35 mg. per 100 c.c., or phenolsulphonphthalein excretion of less than 20 per cent indicates very serious renal damage.[22] The impairment of renal function as shown by these various tests indicates the degree of increase of surgical risk. The eyegrounds also may give very important evidence concerning the severity and prognosis of the nephritis.

Following 26 operations on patients with acute nephritis, O'Hare and Hoyt[22] had 2 deaths, one from mercuric chloride poisoning, the other from empyema, and the outlook for both patients was considered probably hopeless before operation. The other 24 had normal convalescence except

for the urinary sediment. The risk for this group of patients therefore is only moderately increased. They should receive alkalis before operation, and while the urinary volume is low operation should be avoided if possible. Among 21 chronic nephritic patients, with high blood pressure and seriously impaired renal function, the same authors report a mortality, namely of 33 per cent. These patients should receive alkali for three days before operation and the daily urinary output should be kept above 1500 c.c. by forcing fluids. Even under most favorable circumstances, operation on this group of patients is hazardous.

THYROTOXICOSIS

Death from postoperative thyroid storm may be prevented in all but the most seriously sick patients if it is realized that each of the following factors is of unfavorable prognostic significance: age of forty years or over; duration of disease greater than one year; loss of one-fifth or more of the body weight; failure to gain weight during the preoperative period of rest and iodine treatment; failure of the pulse rate to drop to 100 or below during the preoperative period; high basal metabolic rate before treatment, and failure of the rate to show a good drop under treatment to a level less than plus 50; vomiting or diarrhea; marked physical restlessness; and failure of preoperative narcotics to produce the usual sedation. The grading of surgical risk is in accordance with the number and severity of these adverse factors. In the case of each seriously sick patient it should be decided before operation whether the entire surgical procedure may safely be done at one time or should be divided into two or more operations. If the latter course is chosen, it should be adhered to rigidly, even though the pulse rate, the pulse pressure and the oxygen consumption during operation indicate a favorable course.

The risk presented by the so-called apathetic thyroid patient is perhaps not so generally recognized. These patients are elderly, have had the disease a long time and have lost much weight. Many of the signs of thyroid toxicity have long since disappeared, as if the fire had burned itself out: the demeanor is calm, the pulse rate may be slow and the basal metabolic rate only slightly elevated. In spite of apparent non-toxicity and in spite of a most favorably appearing course on the operating table, thyroidectomy in these patients must be divided into two stages, and every supportive measure must be given in order to prevent gradual waning of strength and life after operation. Death occurs in these patients without any sign of a relighting of thyroid activity such as is seen in patients in the common stimulated phase of thyroid toxicity.

The danger of pressure from thyroid tumors has been considered in the section entitled "Oxygen Metabolism."

MISCELLANEOUS FACTORS

Addison's disease marks the patient as presenting at least grade 3 risk.[5,18]

The *chronic alcoholic* is more susceptible to postoperative complications than others. With operations of an emergency nature, the usual intake of alcohol had better be maintained, lest sudden withdrawal cause cerebral edema. When plenty of time is available the patient should undergo a "cure" and be prepared for operation by plentiful intake of carbohydrate.

The presence of any *infection* in the body would seem to increase the likelihood of postoperative infections, the degree of risk depending on the location and severity of the infection, from peridental sepsis at one extreme to overwhelming septicemia at the other. Statistics from the Wisconsin General Hospital[36] show that with cyclopropane anesthesia both major and minor postoperative respiratory complications were three times as frequent in patients with preoperative respiratory complications as in those without preoperative respiratory complications. With ether anesthesia there was not this difference, but all figures were high.

Asthmatic patients as a whole withstand anesthesia and operation very well. Etherization is sometimes followed by a prolonged period of freedom from asthmatic attacks, and accessory drugs such as morphine, ephedrin and epinephrin give temporary relief.

One major operation should not follow another *recent major operation* too closely. It should be borne in mind that widespread, persistent, marked deviations from normal of the functions of many systems are produced by apparently simple operative procedures and by even the less harmful of the anesthetic agents. Unless sufficient time elapses between two major operations to allow the patient to resume his normal activities and to regain his normal vigor and appetite, the risk of a second operation is definitely increased.

COMMENT

Technically difficult or laborious procedures are not usually required for an approximate estimation of the anesthetic risk. Four of every five dangerous situations will be detected, and clues to the fifth will be obtained from minimal data concerning the patient's age, strength, glycogen reserve, cardiovascular symptoms, urinalysis, and hemoglobin content of the blood. These require but a brief visit of inspection and questioning, and some degree of medical experience and judgment, in addition to the simple laboratory tests made. The further details of history, physical examination, special examinations, and laboratory data will often throw additional light, should usually be available, and should always be obtained where the minimal data indicate that they may be helpful.

With the exception of chloroform, any of the commonly used anesthetic agents and methods is reasonably safe for almost every patient. However, the pathological state of the patient is only one of the hazards that lurk in the vicinity of the operating room. Fully as important in the ultimate outcome are the surgeon and the anesthetist. The former obviously has abundant opportunity to run into trouble, and a careless or poorly trained anesthetist may lead a patient to his death when every other circumstance favors complete recovery. He may administer ether too rapidly and thus induce respiratory complications. He may fail to observe or evaluate the signs of shock or to institute measures to combat it. He may permit spinal anesthesia to run too high and may fail to administer artificial respiration. He may permit respiratory obstruction to develop with resultant complications or death, immediate or late. Every general hospital should provide a place for, and every surgeon should see that his patients have the services of, a competent anesthetist. It may even be said that *the skill of the anesthetist is the most important factor in the determination of the anesthetic risk.*

SUMMARY

Careful preoperative estimation of the anesthetic and surgical risk will aid in the avoidance of many pitfalls. A scale for grading the degree of risk is presented. The estimation of the risk and the methods to be used to lessen or compensate for it are considered under the topics of weakness, prolonged invalidism, the psychic state, nutrition, acidosis and alkalosis, oxygen metabolism, the cardiovascular system, hepatic insufficiency, diabetes, renal insufficiency, thyrotoxicosis and minor miscellaneous topics.

REFERENCES

1. Allan, Frank N. Surgery and diabetes. *Surg. Clin. N. Amer.*, 13: 719–725 (June) 1933.
2. Butler, S., Feeney, N. and Levine, S. A. The patient with heart disease as a surgical risk. *J. A. M. A.*, 95: 85–91 (July 12) 1930.
3. Derow, H. A. Significance of postoperative rises of blood nonprotein nitrogen. *New Eng. Jour. Med.*, 212: 509–511 (Mar. 21) 1935.
4. Faught, F. A. Blood pressure evaluation of the surgical risk from the internist's viewpoint. *Anesth. and Analg.*, 10: 227–232 (Sept.-Oct.) 1931.
5. Gordon-Taylor, G. Bad surgical risks. *Brit. Med. Jour.*, 2: 755–760 (Oct. 27) 1934.

6. Henderson, Y. The time that the breath can be held as an index for acidosis. *J. A. M. A.*, 63: 318 (July 25) 1914.
7. Herrmann, G. and L. G. Cardiac disorders in surgical patients: criteria used in estimating the risk involved. *Texas State Jour. Med.*, 30: 183–191 (July) 1934.
8. Hickman, J., Livingstone, H. and Davies, M. E. Surgical and anesthetic risk in cardiac disease. *Arch. Surg.*, 31: 917–936 (Dec.) 1935.
9. Horine, E. F. Anesthesia in heart disease. *Anesth. and Analg.*, 13: 129–131 (May-June) 1934.
10. Hussey, F. V. Estimation of and methods of meeting surgical and anesthetic risks and post-operative complications in surgical diseases of the biliary tract. *Anesth. and Analg.*, 14: 263–269 (Nov.-Dec.) 1935.
11. Ivy, A. C., Shapiro, P. F. and Melnick, P. The bleeding tendency in jaundice. *Surg., Gynec. and Obst.*, 60: 781–784 (April) 1935.
12. Joslin, E. P. The diabetic patient and his condition preparatory to anesthesia. *Anesth. and Analg.*, 8: 61–63 (Jan.-Feb.) 1929.
13. Klotz, O. Influence of some chronic pulmonary lesions on anesthesia. *Anesth. and Analg.*, 12: 122–125 (May) 1933.
14. Lashbrook, E. E. A comparison of Froe's, Moot's and energy index coefficients. *Anesth. and Analg.*, 8: 58–61 (Jan.-Feb.) 1929.
15. Lidwill, M. C. Cardiac disease in relation to anesthesia. *Anesth. and Analg.*, 9: 145–150 (July-Aug.) 1930.
16. McClure, C. W. and Peabody, F. W. Relation of vital capacity of lungs to clinical condition of patients with heart disease. *J. A. M. A.*, 69: 1954–1959 (Dec. 8) 1917.
17. McKittrick, L. S. and Root, H. F. Diabetic surgery. Philadelphia, Lea & Febiger, 1928.
18. McQuiston, J. S. The relationship of arterial hypotension to surgical risk. *Jour. Iowa State Med. Soc.*, 25: 331–333 (July) 1935.
19. McQuiston, J. S. and Allen, E. V. The relationship of arterial hypertension to surgical risk. *Collected papers of the Mayo Clinic and the Mayo Foundation*, 24: 467–476, 1932.
20. Miller, A. H. The influence of age in surgical prognosis. *Am. Jour. Surg.* (Anesth. Supplement), 33: 112 (Oct.) 1919.
21. Moersch, H. J. Vital capacity in relationship to surgical risk. *Anesth. and Analg.*, 7: 262–264 (Sept.-Oct.) 1928.
22. O'Hare, J. P. and Hoyt, L. Surgery in nephritic and hypertensive patients. *New Eng. Jour. Med.*, 200: 1292–1295 (June 20) 1929.
23. Peabody, F. W. and Wentworth, J. A. Clinical studies of respiration. *Arch. Int. Med.*, 20: 443, 468 (Sept.) 1917.
24. Phelps, A. E. Coronary heart disease in surgical patients. *Anesth. and Analg.*, 8: 291–293 (Sept.-Oct.) 1929.
25. Rodman, J. S. and Leaman, W. G. The surgical risk with special reference to the cardiovascular system. *Annals Surg.*, 103: 13–23 (Jan.) 1936.
26. Rowntree, L. G. The renal phase of surgical risk. *Annals Surg.*, 103: 24–28 (Jan.) 1936.
27. Ruth, H. S. The routine evaluation of surgical and anesthetic risks. *Anesth. and Analg.*, 5: 16–20 (Feb.) 1926.
28. Sevringhaus, E. L. Guide for Diabetics, with Suggestions for their Physicians. Madison, Wisconsin, 1935.
29. Stange, V. A. Prognosis in general anesthesia. *Russky Vrach*, 13: 73 (Jan. 18) 1914; abstract in *J. A. M. A.*, 62: 1132 (April 4) 1914.
30. Studley, H. O. Percentage of weight loss: a basic indicator of surgical risk in patients with chronic peptic ulcer. *J. A. M. A.*, 106: 458–460 (Feb. 8) 1936.
31. Sykes, W. S. The evaluation of operative risk: a criticism. *Anesth. and Analg.*, 13: 99–101 (May–June) 1934.
32. Thalhimer, W. Laboratory aid for complications in abdominal surgery. *J. A. M. A.*, 89: 1845–1847 (Nov. 26) 1927.
33. Thalhimer, W. Laboratory aids in the preparation and after-care of surgical patients. *Anesth. and Analg.*, 7: 30–33 (Jan.) 1928.
34. Waterman, A. H. The internist's problem in anesthesia. *Anesth. and Analg.*, 6: 109–116 (June) 1927.
35. Wells, C. J. Preparation of the patient. *Anesth. and Analg.*, 7: 257–262 (Sept.-Oct.) 1928.
36. Wisconsin General Hospital, Department of Anesthesia: Statistical Report for 1935. Page 41, Table VI-K. (Privately printed.)

CHOICE OF ANESTHESIA*

L. F. Sise, M.D.

BOSTON, MASSACHUSETTS

THERE are very many factors which may influence our choice of an anesthetic agent, but the chief of these must always be the safety of the patient and, to a lesser degree, the efficiency of the anesthesia. Among the many lesser factors are the comfort of the patient, the equipment and facilities available and the qualifications of the anesthetist and surgeon.

We will review briefly the present anesthetic agents and methods in use and then see how the condition of the patient and the type of operation affect our choice, always having in mind safety and efficiency. The criterion of choice is the end result of anesthesia and operation combined and not considerations concerning the anesthesia alone. For example, nitrous oxide is generally acclaimed as a non-toxic and safe anesthetic; but in abdominal surgery it may well prove more dangerous than some more powerful anesthetic, because it gives such poor operating conditions that surgical complications may result. Here then the end result of anesthesia and operation may be worse than where an anesthetic more favorable to the surgery is used, even though that anesthesia taken alone and by itself may be more dangerous.

ANESTHETIC AGENTS

Ether. It is most fortunate that ether was the first anesthetic agent discovered and in general use, since it has immediate safety, is powerful and is easy to give. It has, however, numerous toxic actions. It depresses the functions of the liver and produces tissue changes in this gland. It depresses sometimes severely the function of the kidneys and may produce tissue changes here also. It raises the blood sugar, may produce acidosis and causes postoperative nausea and vomiting. Locally it is an irritant to the respiratory tract and may tend to the production of postoperative pulmonary complications. It is also inflammable. Because of these undesirable features, other forms of anesthesia are usually preferable. Ether, however, is very valuable when used in conjunction with the gases and also when other forms of anesthesia are difficult to apply.

Chloroform is the most toxic of all inhalation anesthetics. It is dangerous during administration, it has severe toxic action on the liver, and less on the kidneys and heart. There are so many other forms of anesthesia having little or no toxic action that this agent should be avoided as far as possible and should never be given under conditions, such as starvation, in which liver damage can be produced more readily than usual. Its chief advantage is that it is non-inflammable.

Ethyl chloride has a toxic action similar in character to that of chloroform, but less severe. In this respect it stands between ether and chloroform. Its anesthetic action is very rapid and powerful. It, therefore, has great possibilities of danger and requires an administrator who is well skilled in its use. Its chief advantage is its extreme rapidity of action. An almost equal rapidity of action, however, may now be obtained by means of vinyl ether; and as this is a safer drug than ethyl chloride, it should be used in preference to it.

Vinyl ether is highly volatile, rapid in action and only slightly irritating. It has some toxic action on the liver and tends to the production of mucus, and occasionally gives rise to muscular excitement. It is quite powerful and induces rapid anesthesia followed by quick recovery. It is, therefore, good for short anesthesias re-

* From The Lahey Clinic.

quiring considerable relaxation, and makes an excellent induction for ordinary ether anesthesia. It should not be used in long procedures, over one-half to one hour, according to depth, since there is too much question of its action on the liver. Because it requires little equipment, is easily portable, is rapid and powerful in action, it is a very convenient anesthetic.

Nitrous oxide is the weakest of all inhalation anesthetics. Its chief value is that it is non-inflammable. It is generally considered to be non-toxic and very safe; but the margin between anesthesia and asphyxia is quite narrow. Therefore, it is difficult to give and requires an expert in its use. It is practically impossible to give pure nitrous oxide-oxygen anesthesia without some degree of anoxemia. Anoxemia in itself is toxic and greatly intensifies the toxic action of any other agent which is being used. Anoxemia may be lessened or even eliminated by the use of heavy preliminary medication or of some agent such as tribromethanol or by the addition of some agent such as ether; but in these last two cases, a toxic agent is added, making the avoidance of anoxemia doubly important and, in the case of ether, making the mixture possibly inflammable and explosive. These combinations, however, give an excellent anesthesia which is flexible and comparatively non-toxic.

Ethylene is similar in its action to nitrous oxide but more powerful and can, therefore, be used with more oxygen. It is, however, inflammable and in some mixtures explosive. Up to the arrival of cyclopropane this was the least toxic of our inhalation anesthetic agents. It is now, however, being displaced by the more powerful cyclopropane which is superior to it for most purposes.

Cyclopropane. We are indebted to Henderson and Lucas, and to Waters and his associates for the newest and in many ways the best of our inhalation anesthetic agents. It is a powerful gas, effective with a large amount of oxygen. Those who use it for the first time, should do so with great caution because it is so powerful as compared with the other gases, it being effective in approximately 15 per cent concentration. It has a wide margin of anesthesia without anoxemia. Its toxicity is low, having little or no action on liver, kidneys or acid-base balance. It has, however, a depressive action on the vascular system and probably some toxic action on the heart muscle. Fatal ventricular fibrillation has been produced by its action in dogs, but only with very high concentrations, far above those used for anesthesia. It has a rather marked tendency to the production of extrasystoles. It is depressing or at least non-stimulating to respiration. It is inflammable and moderately explosive. It is quite expensive per unit as compared with the other gases so that the carbon dioxide absorption method of anesthesia is the only one practical for its use. With this method, however, its total expense compares favorably with that of other anesthetics. It is a very valuable anesthetic because of its power, its low toxicity and the large amount of oxygen which may be used with it. This makes it particularly valuable in chest operations.

Where "gases" are referred to in this paper, any of the three gases, nitrous oxide, ethylene or cyclopropane is indicated but cyclopropane is considered superior to the other two unless otherwise stated.

Tribromethanol. This drug is mildly toxic to the liver and kidneys and should not, therefore, be used under conditions in which damage to these organs may be readily produced. In safe dosage it is a very weak anesthetic agent and, therefore, suitable only for basal anesthesia or possibly very light complete anesthesia. It is depressing to respiration and circulation. It is not apt to be followed by postoperative nausea and vomiting.

The barbiturates may be conveniently divided into long acting and short acting. The long acting barbiturates are suitable only as part of preliminary medication or as hypnotics. The short acting barbiturates may be given in the same way but are use-

ful also intravenously as a complete anesthetic. We have had experience with but two, "evipal" and "pentothal." These are depressing to respiration and circulation, otherwise they have little toxic action. Absence of nausea and vomiting is conspicuous after their use. They are useful for a short deep anesthesia or for a more prolonged lighter anesthesia and seem more useful than tribromethanol since they are under much more definite control. But accumulated experience of different individuals is not yet sufficient for one to be quite positive about this.

Local Acting Anesthetic Agents. Cocaine is a very toxic drug but is useful for topical application to mucous membranes if only a short anesthesia is desired. Pontocaine and possibly nupercaine are probably less toxic for topical use if a longer anesthesia is desired, but our experience with these two is very slight. Procaine has had the reputation for many years of being the least toxic of the local anesthetic drugs. Local or regional anesthesia by means of procaine is probably the least toxic anesthesia which can be produced.

Metycaine is mentioned but briefly since it is not at present on the market for spinal anesthesia. It is more powerful and longer acting than procaine and is, therefore, usually better for local, regional and spinal anesthesia.

Pontocaine is not recommended for local or regional anesthesia since we have had no experience with its use. It is, however, excellent for spinal anesthesia. While it is probably more toxic than procaine the dose is so much smaller, being about one-tenth that of procaine, that it is less depressing, while at the same time the anesthesia is much longer acting. This less depressive effect may also be due to a distinct difference from procaine in its type of action, namely, a less intense effect on the sympathetic system.

Nupercaine is a quite toxic drug but its action is very powerful and prolonged so that it can be used in extremely small doses as compared with the other drugs, and it is effective in very weak solution. It is not recommended for local or regional anesthesia since we have had no experience with its use. It is, however, extremely effective for spinal anesthesia by the Jones technique since by this method a very prolonged anesthesia may be obtained with a minimum of depressive effects.

Preliminary Narcosis and Basal Anesthesia. Preliminary narcosis is a valuable aid to all anesthetic agents and may even be used, in part at least, as an anesthesia in itself. In fact there is no sharp dividing line between narcosis and anesthesia. By variations of the narcotic drugs and their doses different states of the sensorium may be produced which vary all the way from a hardly perceptible dulling to an effect which amounts to complete anesthesia of considerable depth. This subject is definitely a part of the anesthetic technique.

METHODS

Carbon Dioxide Absorption. This method makes possible a tremendous saving in the amount of anesthetic agent used and also induces quiet respiration. The close confinement of inflammable anesthetic gases within the closed system makes their ignition more difficult. It should therefore be used whenever possible. The quiet respiration is especially valuable in chest and abdominal operations and to a less extent in neck operations.

Intratracheal anesthesia gives assurance of a clear and non-obstructed airway and thereby promotes quiet respiration. It is valuable in chest operations because it promotes quiet respiration and because it is possible to control pulmonary pressure accurately; in abdominal operations because of the quiet respiration and the impossibility of causing laryngeal spasm; in neck operations where obstruction may be likely, as with intrathoracic goitre; and in head and neck operations because the anesthetist may then be out of the way and yet be assured of a clear airway. It is probably not wise to use it with pulmonary

tuberculosis because of the possibility of inducing laryngeal tuberculosis.

Pharyngeal anesthesia may be used either through the nose or the mouth. It may be given with to and fro respiration with one of the gases or with ether, or by insufflation with ether. It is useful in operations about the head where the anesthetist must be out of the field of operation, where a mask cannot be applied to the face or where the mouth must be open.

Regional anesthesia exerts virtually no toxic action on the various organs of the body and is therefore usually followed by a better postoperative recovery than is any other anesthetic. It should therefore be used when practical. However, it is time consuming and occasionally is insufficient in depth or extent so that it has to be supplemented by a general anesthetic, and it may require self control both by the patient and the surgeon.

Spinal anesthesia, while in reality a form of regional anesthesia of a nerve block variety, will, for convenience in wording, be considered separately in this paper because it presents characteristics which are quite different from other forms of regional anesthesia. By its means, with a simple technique and a comparatively small dose of the drug, an anesthesia may be produced which may be made quite extensive and which is suitable for a wide variety of operations below the diaphragm. Toxic action on the tissues is very low because of the small amount of the drug used in proportion to the extent of the anesthesia. Unfortunately it has inherent in itself certain elements of danger which are not present in regional anesthesia and which call for special caution in its use. For many years the bugbear of this method has been the drop in blood pressure which occurs with its use and the ever present fear that it might lead to a fatality. There has been, however, such a steady advance in perfecting this method that at the present time, if the anesthetist is well skilled and experienced, the risk of such a mortality is practically negligible. Its chief drawback is rather a possibility of nerve complications. Serious complications, however, are quite rare. In our cases of spinal anesthesia, which number approximately 6000, nerve complications have been few, minor and temporary.

The advantages of spinal anesthesia are very great, as it produces extreme muscular relaxation, lacks toxic action on the various organs of the body, and is followed by an excellent recovery which is without nausea and vomiting. Nervous patients should receive rather heavy preliminary medication, or may be made unconscious with cyclopropane. This drug is very appropriate for this purpose because of the high amount of oxygen which may be used with it, and because of quietness of induction. On the whole the advantages of spinal anesthesia appear far to outweigh its disadvantages. It is particularly valuable in abdominal and rectal operations because of the extreme relaxation produced. It is useful in genitourinary surgery because of its lack of toxic action on this tract. It may be useful in bone and joint surgery of the lower extremities where extreme relaxation is necessary, such as in tendon transplantation.

Rectal anesthesia may be given by the rectal instillation of certain drugs such as ether-oil, tribromethanol, paraldehyde or the short acting barbiturates. This anesthesia lacks any real measure of control, so that it is unsafe to produce any but a very light plane of anesthesia, and reenforcement with some other anesthetic is usually necessary. It is pleasant to take and is usually followed by a good recovery with a minimum of nausea and vomiting. It is suitable chiefly as a basal anesthesia but may be used also for the very lightest plane of full anesthesia.

Intravenous anesthesia has recently made a great advance because of the arrival of the really short acting barbiturates. Their action is so short that anesthesia is subject to a large measure of control not possible with longer acting drugs. They are used chiefly for a short deep anesthesia but may

be used also for a prolonged lighter anesthesia. This anesthesia is followed by an excellent recovery with the least nausea and vomiting following any general anesthetic. The short anesthesia may be used for almost any short operation. In our experience these have been manipulations, reduction of fractures, opening abscesses, dilatation and curettage, and encephalograms. The more prolonged anesthesia we have used as yet in a limited number of cases, but have been very pleased with the results in such operations as spinal fusion, sacroiliac fusion, laminectomy and other bone and joint operations up to four hours, as well as in ventriculograms and craniotomies. For this purpose we have used an intravenous saline drip and have added the anesthetic agent as needed by puncturing the rubber tubing near the intravenous needle.

Helium mixtures are useful in cases of respiratory obstruction. The density of helium is 0.138 as compared with 1 for that of air. It has the smallest specific gravity of any element with the exception of hydrogen, but unlike hydrogen it is non-inflammable. Thus helium will "thin" or lower the density of any gas with which it is mixed, with the exception of hydrogen. Thus it has been demonstrated that an artificial air composed of 79 per cent helium and 21 per cent oxygen can be moved in greater volume and at the same time with less force or effort through a given aperture than can ordinary air. This artificial helium air has been used therapeutically with success in conditions of respiratory obstruction or fatigue such as asthma or pneumonia.

The addition of helium to any of the ordinary mixtures of inhalation anesthetics produces a similar effect, and enables larger volumes of these mixtures to be breathed through a constricted opening and with less effort by the patient. Thus it is of value in all cases of respiratory obstruction.

The use of helium, however, is not a panacea for obstructed breathing, and especially it is not a substitute for a clear airway. This latter still remains a prime consideration in inhalation anesthesia and only when it cannot be obtained should resort to helium be made.

For the purposes of this discussion obstruction to respiration may be divided into two classes, slight obstruction and severe obstruction. Where, in spite of best efforts to secure a clear airway, slight obstruction still remains, if the procedure is not so prolonged that intratracheal anesthesia is felt advisable, helium may be added to the anesthetic mixture to relieve the patient's breathing for the remainder of the procedure. Some benefit is obtained, but the results are not striking.

It is in the second class, the severe grades of obstruction, that the most striking results are obtained. But here, the obstruction being severe at the start, even after considerable relief the breathing is not sufficiently free to proceed for long, so that usually there should be resort to intubation. The helium has its use in the interval before this can be accomplished. In our experience the benefit of helium has been demonstrated most strikingly in cases coming to the operating room with obstruction of marked degree from pressure on the trachea or from paralysis of vocal cords. Here helium has been used simply during the induction of general anesthesia for purposes of intubation. A mixture approximating 79 per cent helium and 21 per cent oxygen has first been used and then cyclopropane has been added to this. The breathing at first becomes easier as the helium mixture is applied but becomes more difficult as the heavy gas cyclopropane is added. The relief afforded by the helium, however, has been sufficient to make possible this second period of induction of anesthesia and intubation. The helium has thus afforded relief during a period when otherwise asphyxiation would have been close at hand.

CONDITION OF PATIENT

Respiratory Disease. Operations on patients having respiratory disease as a

complication should be avoided if possible. Where operation is necessary regional and spinal anesthesia are probably most suitable, but even the use of regional anesthesia by no means guarantees freedom from postoperative pulmonary complications. Open ether anesthesia is probably least desirable to use. It is to be remembered that the effect of other factors, such as the site and type of operation or the presence of sepsis, is far greater than is that of the choice of anesthesia on the incidence of postoperative pulmonary complications. If regional or spinal anesthesia is unsuitable, the gases or even the gases with a moderate amount of ether produce very little effect on the incidence of these complications.

Vascular Disease. In *hypertension* it is preferable to avoid a rise in blood pressure such as frequently occurs with inhalation anesthesia. Either spinal or regional anesthesia are suitable in the essential form but if there is arteriosclerosis spinal anesthesia may be too depressive, and should be avoided if the sclerosis is extreme. Tribromethanol with one of the gases, or with ether, is often suitable; but with tribromethanol, also, caution must be used in the presence of sclerosis. In *hypotension* the choice of anesthesia usually depends on other factors, such as the patient's general vigor and the site of operation. Inhalation anesthesia is usually suitable. Spinal anesthesia should be avoided in shock and in the seriously debilitated but is well tolerated by the robust person with normally low blood pressure.

Heart Disease. Valvular disease without serious myocardial involvement affects the choice of anesthetic very little if there is not decompensation, and even with mild decompensation offers surprisingly little difficulty with all forms of anesthesia. Spinal anesthesia is very suitable, as well as regional anesthesia if excitement is avoided. Cyclopropane is also extremely useful when deep anesthesia is not necessary, since clinical experience seems to show that in such cases the value of abundant oxygen outweighs possible toxic effects on the heart such as may occur with high concentrations of the drug.

Myocardial disease with or without valvular trouble offers much less certain ground. Any considerable change of blood pressure in either direction should be avoided. Spinal anesthesia is therefore less suitable, and regional anesthesia becomes the first choice, with cyclopropane probably next, though spinal anesthesia and the gases with ether may also be employed.

Kidney Disease. The gases, regional anesthesia or spinal anesthesia, are quite suitable in these cases although in using spinal anesthesia any marked fall in blood pressure should be avoided with interstitial nephritis, especially in the aged. Ether should be avoided or preceded by morphine. Tribromethanol is not desirable.

Liver Disease. In these cases the diet previous to operation should include sufficient carbohydrate to insure an adequate supply of glycogen to the liver, as this protects to a considerable extent against the injurious effects of toxic agents. Anoxemia should be carefully avoided as this strongly accentuates such injurious effects. There should be a plenteous supply of liquids. These three precautions will do much to protect the liver. Ether or tribromethanol should be avoided. Regional, spinal anesthesia and the gases without anoxemia are most suitable.

Disturbance of Metabolism. In hyperthyroidism preliminary medication should be increased, and quiet should be assured. The gases are quite suitable for these cases, especially cyclopropane because of its large oxygen supply. Regional anesthesia is not quite so suitable as the gases since unconsciousness in these cases is desirable. Ether is unnecessary and upsetting. In general, hyperthyroid cases are more resistant to anesthesia, and hypothyroid cases more susceptible, but with extreme hyperthyroidism the patient may be so weakened as to be quite susceptible. It is to be remembered also that patients with marked degrees of hyperthyroidism may also have

liver damage. Ether should be avoided in diabetics because of its tendency to raise the blood sugar and to upset the acid-base balance. Here regional anesthesia or spinal anesthesia or the gases without anoxemia are quite suitable.

Shock. When shock is present regional or, as a second choice, light gas anesthesia, is to be preferred, ether or spinal anesthesia usually being contraindicated because of their depressing effect on the circulation.

In General. Clinically, young adults seem to require the largest dosage of the various anesthetic agents to produce anesthetic and toxic effects respectively, while the two extremes of life require the least.

SITE OF OPERATION

Abdomen. In abdominal surgery, as the site of operation is reached through a muscular wall and as sensitive structures are frequently encountered, there is need of an anesthesia which will suppress powerful reflexes and produce muscular relaxation. Without such anesthesia the surgeon may be so hampered that his operation may be done poorly or even curtailed.

This need is met admirably by spinal anesthesia. The combination which it affords of extreme relaxation, contracted intestines and quiet breathing, offers operative conditions unrivaled and hardly even approached by any other form of anesthesia. These conditions are especially valuable in the very muscular or obese patient, and in difficult operations such as excision of carcinoma of the rectum, gastric resection, or exploration of the bile ducts, as well as in peritonitis both local and general, where they obviate to a considerable extent the dangers of protrusion of intestines, excessive handling, packing back of viscera, and spreading of sepsis. Moreover the absence of toxic action on the tissues by spinal anesthesia makes it extremely valuable for the patient handicapped by disease of the lungs, liver, kidneys or heart. Under these circumstances we believe the total mortality from anesthesia and operation to be lower and the surgical results better than with any other form of anesthesia. However, spinal anesthesia has certain dangers which require thorough knowledge, experience and constant vigilance if they are to be avoided. Therefore with easy subjects and simple operations where the best operating conditions are not so essential and with patients not handicapped its advantage is less marked and its possible danger becomes of more moment. The question of its advantage is also influenced by the fact that it is more dangerous if high enough for upper abdominal operations than if it is suitable for a lower abdominal operation only. On account of the frequent occurrence of vascular depression it is not suited to those who present a desperate risk, whose pulmonary space is markedly lessened, or whose vigor is seriously diminished as by shock, hemorrhage or prolonged sepsis. Surgical intervention in this latter class of patient is usually very urgent and deep relaxation may well be foregone in order to reduce the burden of anesthesia to the minimum. Here anesthesia by field block is to be preferred with the addition, if necessary, of cyclopropane with possibly a little ether.

Spinal anesthesia should never be given in any event unless administered by one well versed in this procedure. When no such person is available cyclopropane may be given when it will produce sufficient relaxation, regional anesthesia when demanded by the condition of the patient, and ether in other cases. Ether continues to occupy an important place in abdominal surgery. It is well tried and tested, has been the standard for many years, is always available, as it may under necessity be given even by a novice, gives good relaxation, and is safe as regards immediate effects.

Trunk and Extremities. Here deep relaxation is seldom needed so that the gases are quite acceptable for most cases. Tribromethanol is suitable for a very few cases. The barbiturates intravenously cover

a much wider field. Both are desirable because they are pleasant to take and because recovery is excellent with a minimum of nausea and vomiting. The barbiturates intravenously are particularly satisfactory and appear preferable to tribromethanol because of their much better control. Regional and spinal anesthesia may also be used. The latter is desirable in operations on the anus and rectum and urinary bladder because of the relaxation which it produces, also in certain operations on the lower extremities. But in amputations or other operations where sawing and pounding take place the unconsciousness of general anesthesia is desirable.

Thorax. For simple rib resection regional anesthesia is usually sufficient. For thoracoplasty cyclopropane is unsurpassed, since it will produce sufficient depth to control reflex effects, can be used with a large amount of oxygen, is non-irritating, and has a minimum of toxic effect. It has similar advantages when the pleural cavity is to be opened. Here the intratracheal method is indicated to insure a clear airway and definite control of pulmonary pressure. Intratracheal anesthesia, however, should probably not be used in cases of pulmonary tuberculosis.

Head and Neck. For operations where the fields of surgeon and anesthetist can be kept separated, such as operations upon the thyroid, mastoid and cervical lymph nodes, especially when infected, gas anesthesia is well suited. It may also be used for certain operations on the head or nasal or oral cavities by using the intratracheal method, or by using to and fro breathing through nasal or oral airways with appropriate packings to prevent escape of gas.

Superficial operations on the face and head, mouth, nose and nasal sinuses may be done under infiltration, field block, or blocking of the sensory nerves. Field block is well suited for operations on the scalp, cranial vault and brain. Regional anesthesia is also suitable for operations on the anterior aspect of the neck, including esophageal diverticulum, but is difficult and unsatisfactory in the posterior aspect. Pharyngeal insufflation of ether vapor is convenient for operations in the mouth or nose, or where the mouth may have to be opened, as in operations for thyroglossal cysts, since anesthesia is easily maintained under these conditions, there is a minimum of anesthesia apparatus to interfere with the surgeon, and the anesthetist may be well removed from the field of operation.

In operations of any magnitude, such as brain operations, where there are several people in the operating group, it is an advantage for the anesthetist to be well out of the way. This may be achieved by using insufflation of ether vapor, but if the operation is to be prolonged it is better to avoid the prolonged effects of ether. Here gas may be given by the intratracheal route with to and fro breathing and carbon dioxide absorption. Breathing tubes of double the usual length may be used without material difficulty in order to place the anesthetist at a distance from the field of operation; or one of the short acting barbiturates may be given intravenously, and would be especially useful if diathermy is being used, because of complete safety from fire and explosion hazard. Intratracheal anesthesia with the gases using an inflatable cuff or suitable packing is also desirable in operations in the mouth, throat or nose, since inhalation of blood and detritus is thereby prevented.

Where Cautery or Diathermy Is to Be Used. The increased use of diathermy presents a problem for inhalation anesthesia, since the best of these anesthetics are inflammable. Diathermy may be more dangerous than the actual cautery since sparking may occur at points distant from the electrode in actual use. Where some form of anesthesia other than inhalation such as regional, spinal, rectal or intravenous anesthesia cannot be used an attempt should be made to use a non-inflammable inhalation agent. Nitrous oxide is often sufficient in combination with tribromethanol. It is to be remembered, however, that if more than a small amount

of ether is added to nitrous oxide the mixture becomes inflammable and explosive.

Where none of these anesthetics will be sufficient and an inflammable inhalation anesthetic therefore has to be used certain precautions will lower the chances of its ignition. The carbon dioxide technique should be used and special care should be taken to see that the mask makes a perfectly tight fit with the face. If there is any doubt on this point a wet cloth around the juncture of mask and face should be used and the breathing bag should be kept deflated.

Where diathermy is used the instrument should be polarized to prevent miscellaneous sparking. If the machine cannot be successfully polarized and sparking therefore still occurs a metallic connection should be made by means of large conductors as short as possible between the negative plate and table and between the table and gas machine and anesthetist. The negative plate should be near the field of operation and its contact with the patient should be made of low electrical resistance. Connection of the table to an outside ground may be necessary. However, high frequency electrical currents are difficult to control. These measures, while helpful, cannot be relied upon to prevent miscellaneous sparking as they can where ordinary static charges only are concerned. Thus the administration of explosive mixtures of inhalation anesthetics in the presence of diathermy remains fraught with possibilities of danger.

In this connection it is to be remembered that ethylene mixtures are non-explosive, though inflammable, in their upper range such as are used for induction, and probably through operation, unless basal anesthesia or much preliminary medication has been given. But the mixtures become explosive as oxygen or nitrous oxide is added. Therefore it is unwise to use the combination with nitrous oxide or to flush the patient with oxygen toward the end of operation. When the mask is removed and the percentage of ethylene is thereby lessened the patient passes very rapidly through a period where the exhaled gases are highly explosive. Therefore special care should be taken at this time. The usual mixtures of cyclopropane are mildly explosive but are especially so with the stronger mixtures such as are used for induction, and become less so as the strength of the anesthesia is lessened, and cease almost immediately as the mask is removed. Thus the action of cyclopropane mixtures is just the opposite of those of ethylene.

SUMMARY

The larger number of anesthetic agents and methods now available make the choice of anesthesia more difficult and confusing but assure the possibility of a more suitable choice than ever.

While there are a multitude of factors which may influence the choice of the anesthetic in each case, yet in general the choice is governed by a few broad considerations. Of these the safety of the patient is paramount.

Of the more commonly used drugs and methods regional and spinal anesthesia are least toxic and ether most, while chloroform is so toxic as practically to preclude its use.

For abdominal operations spinal anesthesia is preferred where technical difficulties are anticipated and field block, or intratracheal gas, or gas ether with field block, for patients in poor condition. Ether is still a good anesthetic especially where equipment is lacking and a skilled anesthetist is not available.

For most operations on the trunk and extremities the gases are satisfactory. The barbiturates intravenously are excellent, and tribromethanol is effective for a few operations where only the lightest anesthesia is necessary. Spinal anesthesia is indicated in a few operations especially on the anus and rectum and urinary bladder.

For operations on the head and neck the gases or regional anesthesia cover most cases. The field of the surgeon and anesthetist may be kept separate by the use of intratracheal anesthesia, pharyngeal anesthesia or ether insufflation.

PREANESTHETIC MEDICATION*

F. A. D. ALEXANDER, M.D. AND STUART C. CULLEN, M.D.

Anesthetists, Bellevue Hospital

NEW YORK

PROGRESS in making anesthesia safe for the patient is encouraging but the lack of progress in making the patient safe for anesthesia is disturbing. Modern anesthesia is quite as intimately concerned with the protection of the patient from mental discomfort in the preoperative period as it is with his protection from physical discomfort during actual surgical manipulation. The success of any anesthetic procedure is largely dependent upon adequate preanesthetic preparation. Such preparation involves a consideration of an extraordinarily large number of intricately related variable elements.

Several requirements must be fulfilled before the patient is brought to anesthesia and operation in an ideal condition. There should be a minimum of fear of the impending procedure and a maximum confidence of its success. There should be depression of general metabolism and obtundation of reflex irritability without coincident depression of circulation, respiration or disturbance of the normal body compensatory mechanisms. The patient should be fortified against probable or possible untoward reactions particularly characteristic of the anesthesia or operation to be inaugurated.

Efforts to produce this ideal are as old as surgery itself. During the many surgical centuries before the advent of anesthesia, opiates, mandragora and cannibus indica were employed freely to dispel the fear attendant upon the contemplation of surgical procedures as well as to allay pain during the actual ordeal.

The discovery of anesthesia should have obviated the necessity of preoperative sedation, but assurance of a painless procedure is still no guarantee against fear and dread. Thus the essential problem of the ancients has been preserved. In 1869 Claude Bernard[1] demonstrated in laboratory animals the value of preanesthetic preparation by the use of sedative drugs. He showed definitely that the opiates decreased reflex irritability, as well as oxygen consumption and that their use permitted one to establish surgical narcosis with a smaller amount of the volatile agents. From this physiologist's laboratory the fundamental basis of preanesthetic medication was thus established.

With an increasing number of drugs and techniques in use for the production of anesthesia have come new problems in premedication. An understanding of the action of these agents, of their advantages and disadvantages has developed a new conception of the possibilities involved in the use of hypnotic drugs as adjuvants. Preanesthetic sedation has emerged upon a more rational basis. The early empiricism has been largely discarded and a sound, scientific rationale is being substituted.

It is the essential purpose of this paper to analyze briefly the various objects, the attainment of which is the purpose of premedication and to discuss the choice and use of the drugs best adapted to assure them.

The assurance of a fearless, confident psychic state is undoubtedly one of the most important purposes of preanesthetic medication. The necessity for its provision is based on two principles; firstly, fear is definitely established as a potent factor in the production of untoward reaction to anesthesia and operation; secondly, the frightened patient usually retains unpleasant and disturbing memories of the anesthesia and operation which may be dominant factors in his future surgical relationships.

* From the Division of Anesthesia, Bellevue Hospital, New York City.

Records are numerous of patients in good health, posted for minor operations, who have died before any manipulation was instituted, apparently from sheer terror. Most competent authorities place considerable emphasis on the importance of the emotions as an etiological factor in the production of circulatory depression. In the sympatheticotonic type of individual this factor is most evident.

That intense fear of any event or happening creates a lasting undesirable and damaging psychic effect is well recognized. This applies particularly to children for whom too often the use of preanesthetic sedation is neglected. Anesthetists who habitually record an anesthetic history are aware of the influence of previous anesthetic experiences on the attitude of an individual about to be anesthetized. Usually it is the approach or induction of the anesthesia which is remembered unfavorably and very frequently this memory is engendered largely because of the fear of the patient for the procedure rather than any actual painful experience.

Individual variations in the degree of apprehension are great and the character of the outward manifestations almost as variable. Experience is the most valuable asset to the proper interpretation of the actual state of the patient's emotions. The patient who exhibits much external evidence of concern only to subside into quiet cooperation with a small dose of sedative and reassurance is more familiar and less important than the tight lipped, well contained individual who shows little superficial evidence of the well of fear and apprehension within him.

Too much emphasis cannot be placed on the importance of reassurance as an adjuvant to drug therapy in the production of psychic sedation. Instances may be recalled in which the purposes of therapy have been defeated by injudicious conversation or inference of a friend or attendant. Insistence upon a consistent, intelligent effort to inspire confidence in the operating team and the success of the procedure at hand by nursing staffs and other personnel is imperative.

The value of a good night's rest before the day of operation must be stressed. Whether this can best be accomplished in or out of the hospital is a much argued question. The value of twenty-four hours or forty-eight hours hospitalization in providing an opportunity for familiarization with hospital environment and an adequate work-up generally outweigh any other consideration. Every effort must be made to make the patient comfortable, and during this period the referred verbal therapy can be most opportunely practiced. Prescription of a soporific drug to assure sleep during this period may be advisable. It should be supplemented with an analgesic whenever pain is present, if mental and physical comfort are to be obtained.

The classical discussion of Guedel[2] on the role of preoperative medication in its effect on reflex irritability and metabolism is the basis of the modern conception of this subject. It is generally recognized that deviations from normal metabolic activity are reflected in a proportional change in the degree of reflex irritability present. The ideal condition of the patient prepared for anesthesia is one in which metabolism approximates as closely as possible the basal level for that individual. The reduction of metabolism to the basal level necessitates an accurate assessment of the state of the metabolism of the patient before operation and the importance of the existing factors which are known to influence it. It requires an additional knowledge of the action of the various drugs at the disposal of the prescriber and of the nature, time and duration of their effects. While actual clinical tests have been used to determine the metabolic state before anesthesia, they are generally impractical and the analysis rests upon clinical observation and experienced deduction.

No purpose will be served here by an exhaustive discussion of the many factors which may possibly influence the metabolic state of the preoperative patient. There

are, however, some common conditions which play a prominent and consistent part in its control.

Age. The normal metabolic rate varies with the age of the individual. Representing the metabolic rates as Guedel has done with a graph, one notes that there is a sharp increase from birth to one year, following which there is a mild swing upward until the fourth or fifth years. A moderate decline below the original height occurs then until puberty when a rise close to the level of the six year peak is evident. From this age until the alloted three score and ten a gradual decrease in rate is seen until the approximate level at birth is reached. This curve demonstrates the value of considering age in premedication and explains why it is usual to underestimate the sedation necessary for children and adolescents and to overestimate it in the aged.

Fever. It has been estimated that for each degree of temperature above normal there is an accompanying increase of from 6.5 to 7.5 per cent in the metabolic rate. Thus a patient with a temperature of 105°F. might be expected to have an increase of 50 per cent in his metabolism.

Pain. Pain markedly increases metabolism. There is no accurate measurement of the degree of pain and therefore no means of assessing its effect in any given case. Therapeutic tests of the efficiency of analgesics in ordinary dosages will be of definite value in the estimation of the part played by this factor.

Emotional States. Metabolism and reflex irritability are greatly speeded up by fear. There is a "reorganization" of the bodily functions to meet the apprehended event actuated possibly by the secretion of adrenalin, thyroxin or similar substances or sympathetic stimulation such as occurs with such secretion. While the injection of adrenalin experimentally, produces a definite but transient effect on metabolism it is unquestionably true that in the nervous, apprehensive patient the effect, whatever its mechanism of production, is sustained and definite.

Toxemias. Acute septic processes are accompanied initially by a marked increase in metabolism. The duration of this increase depends largely on the general condition of the patient, the presence or absence of debility and the acuteness of the toxemia. Too much emphasis cannot be placed on the importance of the rapid change in metabolism often seen in acute toxic patients. Once the "reserve" of the patient is depleted the metabolic rate may fall very rapidly. In long debilitating toxemias, such as chronic osteomyelitis, the metabolism is likely to be lower than normal. The recognition of the peculiar "washed out" appearance of the patients in these circumstances must remain a question of clinical judgment and experience. Specific toxemias, particularly thyrotoxicosis, influence the metabolic rate in proportion to the severity of the disease. It is common practice to measure the rate directly in these cases.

Combination of Pain, Fever and Acute Toxemia. This combination, so frequently seen in acute appendicitis, acute osteomyelitis, etc., is felt to have a definite effect in increasing metabolism over and above the summation of each individual factor.

Sthenicity. This term might be used in anesthesia to describe the state of the individual's strength or muscular development. Reflex irritability will be increased in the muscular active outdoor type over one of the same age and weight who has had a more sedentary existence.

Metabolism in general is increased in pernicious anemia, decompensated heart disease, hyperthyroidism and hyperpituitarism and tuberculosis. It is reduced in myxedema, hypothyroidism, malnutrition, after long continued bed rest, etc. In leukemia, while the general metabolism is increased, the tolerance for depressive drugs, is diminished.

The practical value of a decreased metabolism and obtunded reflex irritability is generally subscribed to by anes-

thetists. It has been said that "as induction goes, so goes anesthesia." That a quiet, adequately depressed patient is likely to have a quiet, smooth induction of anesthesia is axiomatic. That the excitement stage is seen so infrequently in modern anesthesia is largely owing to the extensive use of preoperative sedation as well as the utilization of rapidly acting agents.

Depression of metabolism near the basal level permits anesthesia to be accomplished with definitely less anesthetic agent. When using nitrous oxide or ethylene without such metabolic depression, it is often impossible to supply a percentage of oxygen necessary to prevent anoxemia and still have a sufficient saturation in the blood to maintain surgical anesthesia. With the more potent agents such as cyclopropane and ether, depression with non-volatile drugs obviates the necessity for a concentration of the anesthetic agent, approaching the toxic level.

The utilization of preoperative administration of drugs to offset particular untoward effects of anesthetic agents or operative stimuli, is of relatively recent development. Investigations of the condition of the autonomic nervous system during anesthesia and operation has introduced a discussion as to the wisdom of the routine use of drugs affecting this system. When there is definite evidence of the effect per se of various agents on the autonomic system and better recognition of particular types such as a sympatheticotonic and the vagotonic, interference with the normal mechanisms afforded by the antagonism of intact parasympathetic and sympathetic systems may be found to be contraindicated.

Barbituric acid derivatives in depressant doses have been found, experimentally, to protect against the convulsant effects of cocaine and its derivatives in overdose or sensitivity. Clinically it is believed that they also diminish the incidence of mild "procaine reaction."

Peripheral vasoconstrictors, notably ephedrine, are used to counteract and prevent severe circulatory depression anticipated with certain agents and techniques.

The conception of utilizing antagonistic preanesthetic drugs has been largely discredited. The most notable example was that atropine effectively counteracted the respiratory depressant effects of the opiates. The development of preanesthetic use of drugs for particular specific protection must depend on the further acquisition of knowledge regarding the effects of the anesthetic agents themselves and in further clinical experience in the extent to which those effects if disadvantageous can be prevented or interrupted by non-volatile drugs given preoperatively.

Drugs. Most efficient of all the drugs employed for preanesthetic medication are the opiates. Properly used they provide psychic sedation and a reduction of metabolism without coincident serious impairment of circulation and respiration or disturbance of body compensatory mechanisms. The opiates are alkaloids and are divided into chemically distinct groups, the phenanthrene and isoquinoline. The more significant in discussion of preanesthetic drugs is the phenanthrene group which includes morphine, codeine and heroin. Morphine, the most important of all the opiates is representative of this group, there being only quantitive differences in their actions. Outstanding properties of morphine are its hypnotic effect, its analgesic effect and its depressant effect on metabolism. The latter action is specific and in this regard morphine exceeds any other drug used in the preparation of surgical patients. A consideration of the factors influencing the metabolism of the patient affords the only basis for the intelligent administration of morphine. Proper doses of the drug must be individualized and should recognize the factors that modify the patient's metabolic activity. Morphine may be given safely either intramuscularly, subcutaneously or intravenously. An important consideration in the administration of morphine is the time element. Maximum effects may be antici-

pated in sixty to ninety minutes following a subcutaneous or intramuscular injection. If given by the intravenous route these effects occur in approximately one-third the time. It is imperative that the drug be given a sufficient time before anesthesia so that maximum effects from it and from the anesthetic agent do not coincide. If doses exceeding 3/8 grain (.022 gm.) are indicated it is safer when administered fractionally. One-half the amount may be given two hours before induction and the remainder added in sixty minutes if the effects justify the additional amount. Unfavorable reactions are due most often to overdosage and are manifested by varying degrees of respiratory and circulatory depression accompanying the narcosis. Immediate treatment is best accomplished with oxygen which will insure oxygenation of the tissue during the depression and tend to eliminate the vicious cycle of asphyxia. Artificial respirations may be necessary. Actual antagonism to the toxic effects of the opiates has been reported following the use of such analeptics as metrazol, coramine, caffeine, etc. Idiosyncrasies to morphine are not common but when present may be expected to result in nausea and emesis characterized by violent and prolonged retching. No entirely satisfactory antidote for this unfortunate occurrence is available, although caffeine is recommended and oxygen inhalations have been used. It is interesting to note that these sequela may occur during and are not eliminated by surgical anesthesia.

Several opium derivatives and synthetic morphine substitutes such as pantopon and dilaudid are used widely. Enthusiastic claims are often made for their superiority but at the present time well controlled clinical or laboratory investigations have not proved conclusively that they should replace morphine.

Paraldehyde. This drug is the product of the linking of three aldehydes. The chief action is hypnosis. The margin of safety between the effective and dangerous dose is great. It does not depress circulation and large amounts are required to produce respiratory depression. It is usually administered by rectum or orally in an amount equal to one dram (4 c.c.) to each fifteen pounds of body weight. The full effect when given by these routes may be expected in thirty to forty-five minutes. It is also used intravenously and is then immediately effective. Respiratory depression does not often follow therapeutic doses. In this respect it provides a definite advantage over other commonly used hypnotics. Metabolism is not inhibited by paraldehyde in a degree comparable to morphine. Paraldehyde has been recommended particularly for chronic alcoholics and for patients with decreased vital capacity. The chief objections to its use are its long action and the offensive odor. Untoward reactions are reported only from excessive doses. Oxygenation and artificial respiration must be maintained until the toxic excess of an overdose of the drug is eliminated.

Belladonna Group. There are several drugs in this group derived from the belladonna and scopola plants. Chief among these are atropine and scopolamine or hyoscine. The latter two are identical drugs. Drugs of this group by their parasympathetic action inhibit secretions. Scopolamine also produces psychic sedation by depressing the cerebral cortex. There are no other indications for the use of these drugs in preanesthetic medication. Atropine stimulates metabolism; scopolamine because it reduces emotional excitement does not. The dose of atropine or scopolamine varies from grain 1/100 (.0006 gm.) to 1/300 (.0002 gm.). Smaller doses are often not effective even in children. These drugs are regularly given subcutaneously and are effective in fifteen to twenty minutes. The effect persists for several hours and it is convenient to administer the drugs with morphine. Once mucus stimulation is established it is inadvisable to administer either atropine or scopolamine because although further secretion is inhibited the mucus already present becomes more viscid

and troublesome. The untoward reactions from scopolamine are manifested by a flushed face, circumoral pallor, tachycardia and rarely uncontrollable excitement. The drug is thought to deteriorate rapidly and toxic reactions most often follow the use of scopolamine that is at least a year old.[3] The use of ampules to market the drug has reduced the incidence of unfavorable reactions to a minimum. The use of tablets containing the drug is not without danger. Apomorphine in less than emetic doses from grain $\frac{1}{40}$ (.0015 gm.) to $\frac{1}{30}$ (.002 gm.) has been found a very useful and satisfactory antidote to the unfavorable reactions occasionally observed following therapeutic doses of scopolamine.[4]

Barbituric Acid Derivatives. This ever increasing series of drugs vary so much among themselves in most every pharmacological and biochemical respect that it is practically impossible to consider them as a group. Barbituric acid, the parent drug, prepared from diethylmalonic acid and urea is not hypnotic. The substituted derivatives are purely hypnotics and vary only in rapidity, duration and degree of action. Other properties are so unlike for the different members of the group that they can only be accurately described for each drug. It is not the purpose here to attempt such descriptions but merely to point out that the indiscriminate clinical use which is all too frequent is never justified. The barbiturates produce hypnosis by depressing the central nervous system, particularly the higher cerebral centers. They are not analgesic and given in the presence of pain may cause excitement. During recovery when the higher centers are still depressed, excitement characteristic of a medullary defensive animal may occur.

No group of drugs have been found so variable in their action as the barbiturates. One barbiturate will effect one individual entirely differently from another and the same individual may not react alike to the different drugs. Moreover, experimental criteria for the barbiturates formulated with animals is often not applicable clinically since the variability among different species is marked.

Barbiturates do not decrease metabolism until doses that seriously depress the central nervous system are employed. For preanesthetic medication they are useful to allay apprehension before anesthesia and for medication the night before operation. The barbiturates are also useful to protect against the toxic reactions from local and regional anesthetic drugs.

Barbituric acid derivatives are given intravenously, rectally and by mouth. The latter method has given most satisfactory results for preanesthetic medication. The dose of a barbiturate entails a consideration of the length of action of the drug and its toxicity. The sedative effect desired can only be estimated. The state of health of the individual, his age and weight must be evaluated. It is advised that the determined dose be less than the recommended full therapeutic dose. The intoxication from overdoses of barbiturates has no constant manifestations. Circulatory and respiratory depression accompanying prolonged sleep are most constant. Excitement, vertigo, visual disturbances, febrile reactions, cutaneous eruptions, etc., have been described. Pneumonia and pulmonary edema are to be feared if depression is profound and prolonged. Treatment should include artificial respiration, carbon dioxide and oxygen inhalations, and stimulating drugs. Certain analeptics or antagonistic drugs are recommended, particularly picrotoxin, metrazol and caffeine.

Miscellaneous Drugs. Ephedrine fulfills only one requirement of a preanesthetic agent. It combats the specific circulatory depressant reaction following tribromethanol or subarachnoid anesthesia.

Bulbocapnine has recently been revived and studied experimentally[5] to determine its effectiveness for preanesthetic medication. Its action resembles morphine but it has not been determined as efficient.

Eserine has been used for premedication on the theory that the sympatheticotonic patient may be made less resistant to anesthesia by parasympathetic stimulation.[6]

Of the many valuable drugs available, it is unfortunate that no one will adequately fulfill all the requirements for satisfactory preanesthetic preparation. All too frequently there have been recommended certain drugs to be given routinely for anesthetic preparation. Such premedication cannot be consistently satisfactory and may often be a source of real danger. Individualization for each patient giving consideration to all the factors involved is essential. Such premedication cannot be done by rule or set down in tables of doses for any drug or combination of drugs.

Although the paramount consideration is the patient, one cannot overlook other factors. Anesthetic procedures that appeal to the temperaments of certain surgeons may be demanded. The particular requirements of specific operative techniques cannot be ignored. For example, in intracranial surgery drugs that are known to increase intracranial pressure are to be avoided. In intraocular operations, it may be desirable to use drugs that decrease the intraocular tension.

The anesthetic agent and technique to be employed will influence the choice and amount of drugs employed for preparation. With the relatively less potent agents, more preliminary sedation is desirable. The application of special techniques may be facilitated by proper medication. For instance, if an endotracheal airway is to be placed through the nostril and without direct vision, light surgical anesthesia with a considerable degree of hyperpnea facilitates the manipulation. This desirable condition will not be so readily obtained if the respiratory center is much depressed with non-volatile drugs.

SUMMARY

The use of non-volatile sedative and other drugs before operation to prepare the patient for anesthesia and surgical manipulation is common practice. Preanesthetic sedation is a rational procedure based upon well established principles; these principles have been discussed. The pharmacologic actions of the drugs commonly employed have been described briefly. Factors which may modify the choice of drug, in individual cases, are also presented.

No single drug or combination of drugs can be suited to all cases. Satisfactory results are obtained clinically by various individuals using different drugs, with the same general actions. Experience in the use of any of these drugs, particularly with regard to the adjustment of dose and time factor will result in increasing success. Routine prescription without individualization cannot be satisfactory. The most consistently good results are obtained when the various influencing factors are carefully weighed, the available drugs considered and following the choice and administration, the effects both advantageous and otherwise accurately observed and recorded. The anesthetist, who is thoroughly grounded in the physiologic and pharmacologic principles of sedative drug prescription, experienced in assessment of the varying factors in individual cases, and familiar with the conditions under which the anesthesia and operation are to be performed is best fitted to prescribe sedation for any patient. Training and experience are more often reflected in the success or failure of preanesthetic medication than in any other phase of the anesthetic procedure.

REFERENCES

1. Gwathmey, J. T. Textbook of Anesthesia, N. Y., The Macmillan Co. 1914.
2. Guedel, A. E. Current Researches in *Anesth. and Analg.*, 15: 157–162 (July-August) 1936.
3. Waters, R. M. *Am. Jour. Surg.* Quarterly Supplement of Anesthesia and Analgesia. vol. 119 (Oct.) 1922.
4. Rovenstine, E. A. *Journal-Lancet*, 53: 681 (Dec.) 1933.
5. Molitor, Hans. Current Researches in *Anesth. and Analg.*, 15: 72, 1936.
6. Pascalis, G. *Bruxelles-méd.*, 12: 273–274. (Jan. 3) 1932.

PHARMACOLOGICAL ACTION OF INHALATION ANESTHETICS

HENRY G. BARBOUR, M.D.

Yale University

NEW HAVEN, CONN.

ETHYL ether has been more widely used and more thoroughly investigated than any other inhalation anesthetic and is still certainly the most indispensible. An understanding of the effects of ether affords a key to the pharmacology of all general anesthetics.

After describing the action of ether two other fluid anesthetics, vinyl ether and chloroform, will be briefly discussed, followed by the gas anesthetics, nitrous oxide, ethylene and cyclopropane.

The inhalation anesthetics are, of course, all characterized in their action by widespread and profound depression of the central nervous system. It is convenient to remember that the depression in general appears in the following order: cerebrum (sensation, consciousness, coordination of neuromuscular functions); spinal cord (reflexes); medulla (vascular and respiratory control). In the usual anesthetic death circulatory failure is merely secondary to the collapse of the respiration.

While the anesthetics are in a sense general protoplasm poisons, concentrations which are just fatal in mammals usually exhibit little significant action upon visceral or other vegetative functions. The substance offering the chief exceptions to the last statement is a cardiac depressant and a bearer of damage to parenchymal cells, for which reasons it is fortunately passing into obsolescence. This anesthetic is chloroform.

ETHYL ETHER

The first effects of ether include the appreciation of its pungent odor and taste followed by tinnitus and sensations of "floating", "sinking" or the like, and then by amnesia, analgesia and loss of consciousness. The eyeballs begin to wander and the pupils to dilate but they still react to light, and the conjunctival and corneal reflexes are quite active as the subject passes from the stage of imperfect consciousness to that of excitement.

When the second stage, "excitement" or "delirium," is marked it is characterized by thick rambling speech, excessive muscular activity (coordinated, spastic or both). Whether the excitement stage is due to direct stimulation on the part of the drug or merely to the removal of inhibitions it is certain that this phase of ether anesthesia can break through the depression caused by premedication with such agents as the barbiturates. In this phase of its action ether is therefore definitely antagonistic to sedative agents.

Passing from the stage of excitement to that of narcosis, the pupils begin to grow smaller and blinking or compression of the eyelids is likely to be present. "Voluntary" movements however, soon cease and the skeletal muscle relaxes; the impotence of the limbs becomes such that their support must be looked after to save them from injury.

On passing beyond the first stratum of the stage of narcosis the eyeballs become fixed, the pupils become very small but still react to light and the conjunctival reflex disappears. The other remaining reflexes are likely to disappear in somewhat the following order: corneal, laryngeal, pharyngeal, rectal, vesical, peritoneal, genital and patellar. The vasomotor center becomes depressed before all the reflexes have disappeared, and the blood pressure falls. If the outcome is fatal cyanosis will be followed by pallor and the pupils become fixed in dilation.

The return of dilation of the pupil with the variability in the reflex picture from case to case sometimes leads to doubt as to whether the subject is going into collapse or returning to consciousness. Immediate reduction of the amount of ether, preferably with the addition of high concentrations of oxygen, will soon determine this question, offering at the same time a most important aid against collapse.

Although, as mentioned, the medullary centers are among the last affected the character of the respiration begins to change in the first stage of ether anesthesia. Slow and shallow respiration occurs often with intermittant coughing, retching and vomiting. These changes may be secondary to lung irritation. In the excitement stage the respiration is deep, rapid and irregular while in narcosis it becomes still deeper but regains its regularity. Should the danger zone be reached the breathing becomes rapid and shallow.

The circulation in the first two stages of ether anesthesia is characterized by a rapid pulse rate often associated with a slight rise in blood pressure. These phenomena are attributable to the peripheral irritating effects of the anesthetic. Inasmuch as they promote an increased blood flow and are accompanied by cutaneous vasodilation the result is a pink coloration of the skin. As the action of ether progresses, however, a fall in blood pressure may accompany a rise in the pulse rate. Should both these changes amount to as much as 25 per cent the situation demands a decrease in the anesthetic administration. The blood pressure falls decidedly in the lower strata of narcosis, the inefficiency of the circulation contributing to cyanosis which is worse in case of shock.

The gastrointestinal tract in the induction of ether anesthesia is likely to be involved by the occurrence of swallowing movements, excessive salivation and often vomiting. These all arise from reflex irritation. If the narcosis becomes deep intestinal atony is likely to appear.

In addition to the irritating effects of ether a further action, dependent upon its rapid rate of evaporation, is that of cooling. As is well known this was formerly used as a local anesthetic measure. Inasmuch as the ether is administered in vaporized form the cooling effect of its evaporation from the lungs is more than cancelled by the initial condensation as the gas enters the blood.

The body temperature as a whole is, however, in ordinary environments, significantly reduced by ether, as by all agents which greatly depress the central nervous system. This temperature reduction is due in part to depression of the total metabolism and in part to interference with the vasoconstrictor mechanism. The latter is illustrated by the fact that the soles of the feet are some 5° warmer than usual under ether and that the toes do not chill as normally in response to cold (Sheard and co-workers). These metabolic and vascular changes which cause the loss in temperature are associated with interference with function of the heat regulating centers at the base of the brain. The subject approaches a poikilothermous condition analogous to that induced by the removal in animals of the hypothalamus and higher centers.

The loss of the power to regulate bodily heat is stressed because anesthetized subjects become easily overheated in poorly-conditioned operating rooms. It has been shown that dogs under ether, regardless of the humidity of the environment, will maintain their normal body temperature only when exposed to a temperature very close to 31°C. (88°F.). When this is varied as little as one degree in either direction the body temperature tends to rise or fall as the case may be.

Uncomplicated ether narcosis leads regularly to reduction in kidney secretion and even to anuria. This has been ascribed by some to reflex irritation while others believe that some cellular damage in the kidney is indicated; increased blood concentration may also play a role. Corre-

sponding to these possible factors the oliguria is said to be prevented when ether is administered by mouth, by rectum or intravenously, eliminating irritation of the lungs; it also may be combatted by measures aimed at protecting the kidneys such as alkali and glucose or by giving large amounts of fluid to keep the blood from overconcentrating.

The concentration of the blood in uncomplicated ether narcosis in dogs amounts to as much as 15 per cent. The solids are increased by about 3 per cent (Barbour and Bourne) which is reflected in the red cell count and hemoglobin determination. Partial emptying of the reservoir of red blood cells in the spleen appears to account partly for this change, and there is evidence that discharge of the adrenal glands, which is marked if asphyxial factors are present, plays a role in this blood concentration.

The resistance of the red blood cells to osmosis is also lowered. While the viscosity of the blood as a whole is thus increased that of the plasma is lowered as is its surface tension and refractive index.

The above mentioned depression of the metabolism has been demonstrated in part to occur in the nervous tissue itself; for example, there is less production of CO_2 by the brain. Nerve fibers during ether anesthesia exhibit a preliminary increase of CO_2 before depression. Other metabolic changes are seen in the increase in sugar, urea and non-protein nitrogen of the blood, but of especial importance is the reduction in the alkali reserve. This is associated with some fall in CO_2 tension of the blood but the alkali loss is regarded as unfavorable, sometimes predisposing to vomiting and other toxic manifestations. Prevention by alkali and glucose with insulin is not difficult to secure. In the causation of the alkali loss ketosis, lactic acid production and mobilization of phosphoric acid from the muscles all appear to be significant factors. The acidotic tendency is significant in the parenchymal damage of liver and kidney resulting acutely from toxic concentrations of ether, alcohol and chloroform. As shown by MacNider such effects are preventable by treatment with alkalies, fluid and carbohydrates with insulin. MacNider has also followed the replacement of the cells by a new and more resistant type, and has demonstrated the greater susceptibility of the kidneys in old age.

Absorption and Fate of Ether. Inhaled ether and other anesthetics diffuse readily in either direction through the lung epithelium. The amount taken by the blood is directly proportional to the partial pressure of the gas existing in the alveolar air and to the solubility coefficient for the particular anesthetic. The speed of absorption may be increased decidedly by the induction of deep and rapid respiration by means of the inhalation of CO_2 (Y. Henderson).

The solubility coefficient for ether in the blood is 15, which means that blood equilibrated with air containing ether will hold 15 times as much as will the same amount of air. It may, however, take forty-five minutes or more for the blood to become two-thirds saturated. This is because, during the induction of ether, the other tissues of the body are removing the ether in proportion to their respective rates of blood flow and their capacities to bind ether. Haggard has shown that the degree of saturation of an organ is indicated by the ether content in its venous blood. When equilibrium to the ether concentration in the air is established throughout the body the arterial as well as the venous ether content will indicate the degree of saturation of the various organs. Being thus an index of the amount that the brain is saturated, the arterial blood will indicate the degree of narcosis. But, during ether administration, only that blood which is collected from the internal jugular vein can serve as a guide to the ether concentration in the brain.

The rate of saturation of the brain or any other organ at any given time is proportionate inversely to the solubility

coefficient of ether in the blood and directly to the volume of blood flowing through the organ in question. Haggard points out the fact, favorable for anesthesia, that the central nervous system has a relatively larger blood flow than any other tissue. Its solubility coefficient appears to be the same as that of the blood. He regards the body tissues largely as a huge buffer delaying both the absorption and excretion of ether.

lation is by far the predominating factor in determining the excretion rate.

The control of the respiratory volume by the use of carbon dioxide is valuable because it can increase the rate of induction *without raising the ether concentration* in the air to a highly irritating level. The value of carbon dioxide in facilitating elimination is also great. It may be mentioned that where CO_2 was not available brisk rubbing of the face and lips has been

TABLE I

PHYSICAL AND PHARMACOLOGICAL CHARACTERS OF INHALATION ANESTHETICS

Anesthetic	Formula	Boiling Point °c.	Solubility Coefficients		Effective Concentrations			
					Anesthetic		Lethal	
			Blood Blood/Air Ratio[1] (37°c.)	*Oil* C.c./100 C.c. Oil[2] (20°)	*Air*, Volumes Per Cent	*Blood*, Mgms. Per Cent	*Air*, Volumes Per Cent	*Blood*, Mgms. Per Cent
Ethyl ether	$C_2H_5.O.C_2H_5$	34.6	15.	50	3.7[4] / 4.7[12]	116[5]	4.9[4] / 4.0[3]	154[5]
Vinyl ether	$CH_2{:}CH.O.CH{:}CH_2$	28.3	.....	*	3.9[12]	28[5]	3.8[3]	68[5]
Chloroform	$CHCl_3$	61.2	10.3	265	1.0[6]	24[7]	1.7[9]	40[7]
Nitrous oxid	N_2O	− 88.7	0.43	1.4	95[10] / 2 atmospheres[14]	50[10]	3 atmospheres[14]	
Ethylene	$CH_2{:}CH_2$	−103.9	0.12	1.3	85[13]	.....	140[13]	
Cyclopropane	CH_2 / CH_2——CH_2	− 37	1.15	Easily soluble	25[11] / 13[11a]	.....	39[11]	

* Oil/water partition coefficient is similar to that of diethyl ether.
[1] Compiled by Kochmann.
[2] Meyer, K. H. and Gottlieb-Billroth.
[3] Molitor. Mouse (3 hour anesthesia).
[4] Haggard. Dog.
[5] Goldschmidt, Ravdin et al. Dog.
[6] Rosenfeld. Rabbit.
[7] Buckmaster and Gardner. Cat.
[10] Greene and Currey. Dog; oxygen-lack necessary.
[11] Seevers, Meek, Rovenstine and Stiles. Dog.; [11a], with preliminary morphine.
[13] Leake, Knoefel and Guedel. Mouse.
[13] Halsey, Reynolds and Prout. Mouse, adequate oxygen, lethal concentration with 2 atmospheres pressure.
[14] Lendle. Mouse, adequate oxygen.

The anesthetist can control the amount of ether in the arterial blood regardless of the total ether in the body and this arterial ether is the critical factor for increasing or decreasing brain saturation. The arterial ether content is controlled by the air content and the respiratory volume, and of course is proportional inversely to the blood flow through the lungs.

In the elimination of ether, 87 per cent is accomplished by the lungs; the urine, perspiration and exposed serous surfaces of the body play a minor role. Lung ventiused to stimulate the respiratory mechanism with some success. Of course the depth of the respiration is of much more importance than the rate so far as ventilation of the lung is concerned.

The minimal effective concentrations of ether for producing anesthesia or death are indicated in the table. These figures must be taken as approximations. The conditions under which ether and the other inhalation anesthetics have been studied vary so widely that quantitative comparisons between the results of different

workers are well understood to be dangerous. The reference numbers appended to each figure in our table may be used to indicate with what other figures they are closely comparable. However, in a general way, all of the results may be considered fair indications of what would be likely to hold good in man under conditions of uncomplicated anesthesia.

For adequate surgical narcosis 4 per cent of ether in the air is regarded today as the approximate concentration necessary. Under such circumstances there is likely to be a concentration of 120 mg. in each 100 c.c. of blood. Continued sufficiently long 5 volumes per cent would be fatal, the amount in the blood then attaining about 154 mg. per cent. In the table the figures from ether anesthesia in mice indicate some of the difficulties in comparing with human conditions the valuable studies which are made in this species. It will be noted that one observer requires 4.7 volumes per cent to induce anesthesia; another is able to produce death with only 4 volumes per cent but the administration must be continued over three hours. In this connection it may be noted that in order to prevent unfavorable delay in the induction of ether anesthesia it is found necessary in clinical practice to commence with concentrations which when long continued would be fatal.

Estimation of Safety Factors. The relative safety of inhalation narcotics has defied quantitative estimation through several generations. Too many factors are involved; mortality statistics particularly are contradictory and misleading. Although factors introduced by operative procedures and necessary preliminaries can be excluded by making determinations on normal animals, one is still confronted with such difficulties as comparison between species and the development of methods for determining the amounts and concentrations of anesthesia present in air, blood and tissues.

The "margin of safety" is also difficult to establish, for there are several ways of reducing to a formula the fact that a certain concentration usually suffices to narcotize while another usually suffices to kill. One difficulty is that one must deal with the exceptional cases when talking about the safety factor. For this reason Leake has used standard mice in which the ratio of the lowest concentration producing death in *any* individual is to be divided by the highest concentration necessary to cause anesthesia in *any* individual. Using this criterion he found the minimal lethal concentration of ethyl ether 2.14 times the maximal just anesthetic concentration. Naturally another figure might be obtained from the same set of experimental results by comparing the anesthetic concentration for 50 per cent of the animals with the "m.l.d.50." Conditions like time of exposure have also to be arbitrarily established in making such experiments.

While 2.14 might be the "therapeutic" ratio of ether for mice one may with equal justification derive a "therapeutic ratio" of 1.33 for the dog (see table). Many investigators have referred to the "therapeutic range" of an anesthetic. To arrive at this from the table in the case of the dog one would subtract 3.7 from 4.9 (instead of dividing the latter by the former) and thus arrive at a "therapeutic range" expressed as 1.2 volumes per cent.

To compare other anesthetics, strictly therefore, with ether it would be necessary not only to define the index of safety used but also to correlate a great variety of operative procedures and of premedication effects.

Preanesthetic conditions other than sedation by drugs which may influence the outcome of ether anesthesia are the cardiac reserve, fasting, purgation, dehydration, acidosis, acapnia and psychic or sensory disturbances during induction. Some occurrences during operation which may exert much influence are fluctuating depth of anesthesia, hemorrhage, shock, sepsis, high metabolic rate (as in fever or thyroid cases). Besides this other pathological factors such as cardiac disease, high blood pressure,

anemia, pulmonary inflammation or renal disease may all contribute toward altering the response of the individual to ether.

Premedication. Modification of ether anesthesia by preliminary medication has been the subject of intense study and widely varying practice. The usual aim of premedication is to supply by injection or ingestion a substratum of greater or less intensity, upon which the anesthesia is to be completed with the use of an agent which is inhaled. The effects of an injected drug are not subject to immediate reversal because of the relatively slow elimination of non-volatile substances, whereas the intensity of the effect of volatile substances is largely controllable on account of their rapid excretion. The chief advantage of premedication is the production of some degree of amnesia, analgesia, euphoria and sleep before commencement of the usually unwelcome processes of inhaling a foreign substance through a mask. By lessening the metabolic rate a sedative drug may thereby lessen the demand for oxygen during the anesthesia; it may likewise contribute toward decreasing acidosis, blood concentration and oliguria. Finally it is often desirable to prolong the anesthesia by a period of light sleep following the operation. Furthermore, especially with ether, less variability in the respiration, circulation, etc., occurs after premedication; the anesthesia is "smoother." The irritation of the so-called excitement stage may be eliminated entirely but is likely to break through the sedation to some extent.

"Basal anesthesia" is merely an intensification of premedication to the point of narcosis. No non-volatile drugs exist which may with perfect safety be given to the point of good surgical narcosis; therefore, regardless under what name the preliminary medication is known, the aim should be to attain only sedation. The risk of respiratory depression must be entirely avoided, and the intravenous route used only in emergency. Excess mental or bodily activity before the administration of a sedative tends to detract from its efficiency.

The principal agents used for preanesthetic sedation are morphine, the shorter acting barbiturates, especially amytal and nembutal, scopolamine, tribromethanol (avertin), paraldehyde, chloral and magnesium.

Combination Narcosis. Considerable pharmacological literature has accumulated around the question as to what effect one depressant drug may exert upon the action of another. The much abused term "synergism" was originally designed to indicate that the action of a combination of drugs was greater than could be expected from the summation of the component actions. For example, if one-half of a just narcotic dose of one drug gives narcosis when combined with only one-quarter of the just narcotic dose of another drug, we speak of a true synergic action. There is some evidence that closely related drugs are purely *additive* in their combined action while the combination of two such different substances as morphine and chloroform are synergic. Widely different drugs may select differing sites of action, or one of such a pair may facilitate the penetration of the other drug into the cells. However, in previously untested combinations, there is equal reason to expect antagonism rather than synergism. In the field of anesthesia little has been practically gained from the development of these conceptions. Two superimposed anesthetics usually give merely additive action as shown, for example, by Lendle who obtained this result by varying the proportions of nitrous oxide and ether. Halsey and Lacey, without claiming synergism, have shown that one-fifth the lethal dose of dial or nembutal deepens the narcosis produced by given concentrations of ether. Synergism even when present in therapeutic action loses any advantage if an equal degree of synergism exists in the toxic effects.

On the other hand it is possible to observe antagonism in the toxic effects of the same combination of drugs which produces synergism of therapeutic effects. The theoretical basis of this has been elaborated by Loewe.* No such combination of anesthetics, however, has yet been demonstrated. An example of undesirable combined toxicity of drugs, possibly amounting to synergism, is seen in the fact that the minimal lethal doses both of cocaine and procaine are much lower during ether narcosis.

Stimulation during Ether Anesthesia. A curious anomaly which sometimes develops is the appearance of convulsions during ether narcosis, that is, at a time when most of the central nervous function is depressed much below its normal level. If not epileptic in origin, these convulsions may often be attributed to drugs (especially barbiturates) given for the specific purpose of furthering central nervous depression. Ether does not seem to interfere particularly with the respiratory action of such drugs as atropine and lobeline; the effects of these in any case are rather evanescent. Ether depression seems to yield well to the stimulating action of coramine on the respiratory center.

THEORY OF NARCOSIS

The intimate reaction of ether and other anesthetics upon the cells is too inadequately understood to justify extended discussion here. It will merely be pointed out that the analogy between oil-solubility and narcotic action has received substantial support from many angles. Such an analogy might merely concern transport of the anesthetic to and into the cells, which is not the same thing as the transformation of cellular activity. The Meyer-Overton theory of narcosis has become more substantially grounded by the demonstration that the narcotic concentration in mols per litre of lipoid solvent is a surprisingly constant quantity for a great variety of anesthetics, ranging usually between .04 and .10. In view of the factors of experimental error and the wide differences of 10,000 times in anesthetic potency this is indeed a surprisingly narrow range (V. E. Henderson).

Most of the suggested mechanisms of anesthesia have been found compatible with the lipoid theory and concern such factors as surface tension, absorption, permeability and differences in potential on two sides of a lipoid containing membrane (Beutner). Claude Bernard's theory of reversible semicoagulation of proteins by anesthetics has received considerable attention; by some it has been linked with theories of dehydration, there being evidence that anesthetized cell bodies tend to lose water.

It is clear today that anesthetic action is totally independent of asphyxia although it may lead to the latter condition. When nitrous oxide was the only gas anesthetic in use there was some ground for confusion in this matter but our more modern gas anesthetics function in the presence of complete oxygen saturation of the blood and tissues.

VINYL ETHER

Leake investigated the anesthetic properties of vinyl ether (divinyl oxide) because its chemical formula suggested the possibility of combining the advantages of ether with those of ethylene; how far the expectation of superiority is justified it is still too early to state. Associated with the greater volatility of the vinyl ether appears to be some increase in potency, speed of induction and of recovery. The anesthetic effect of vinyl ether is said to be 140 per cent quicker than that of ethyl ether at 20°C. but only 43 per cent quicker at 35°C.

Apparently vinyl ether does not interfere with the muscular activity of the uterus or the intestine although producing relaxation of the abdominal wall comparable to that of ethylene. During a surgical degree of narcosis with vinyl ether the respiration is strong and the circulation apparently unchanged. There is a low

*Loewe, S. *Klin. Wchnschr.*, No. 23, 1927.

incidence of excitement, postanesthetic vomiting or complications in the lungs and kidneys. It is, however, a marked salivary stimulant, indicating the preliminary use of atropine. Leake's therapeutic ratio for mice is 2.29.

Liver damage when present is moderate and can be traced to anoxemia. Bourne and Raginsky have shown that vinyl ether in normal or fasted dogs does not alter the liver function appreciably; nor does vinyl ether enhance preexistent liver function damage due to chloroform. The same authors attribute death from the anesthetic to respiratory failure, followed closely by failure of the heart. The low concentration of vinyl ether as compared with ethyl ether in the blood (see table) both for anesthetic and for lethal action, is an indication of lower solubility in the blood rather than of higher potency. Vinyl ether is very unstable in pure form but as supplied in commerce is protected by .01 per cent phenyl-alpha-naphthylamine and 3 per cent alcohol.

CHLOROFORM

As shown by the table, chloroform is an anesthetic three times more powerful than ether and more than twice as toxic as judged by the method of minimal lethal concentration. The "therapeutic range," however calculated, is certainly no more favorable than that of ether (Leake's ratio is 1.66) but the relative danger of chloroform as compared with ether lies less in any difference in therapeutic range than in the potency of relatively small amounts.

Most serious is the action of chloroform upon the heart. Here it is effective in concentrations only 3 or 4 per cent as great as are required of ether. Not only is the heart thus exceedingly sensitive to the depressing action of chloroform but in the presence of the drug it quickly develops a most dangerous state of irritability. Fatal syncope may occur in the very first moments of induction.

These facts outweigh all the possible advantages of chloroform over ether such as "smoother" induction (which does not apply when ether is given with suitable premedication) more rapid action, or lesser degree of irritation.

It may be emphatically stated in spite of tradition to the contrary that the use of chloroform as a general anesthetic has no justification today. The deleterious fatty degeneration of the viscera, appearing if chloroform anesthesia is continued for more than a few minutes, serious as it is, is of secondary importance when compared with the danger to the circulation.

GAS ANESTHETICS

The gas anesthetics, nitrous oxide, ethylene and cyclopropane exhibit speedier onset and discontinuance of action than the fluid inhalation anesthetics. At ordinary temperatures this increase of speed is due to their possession of low solubility coefficients in the blood. Narcosis is inversely proportional to solubility in the blood and "inert" tissues (see table) because greater solubility diverts more anesthetic substance from its seat of action.

Two of the three gas anesthetics to be discussed, namely, nitrous oxide and ethylene, are incapable of attaining lethal concentrations at ordinary pressures and are therefore essentially without danger to the patient except in so far as their use entails the occurrence of asphyxia. Cyclopropane, on the other hand, exhibits its own toxicity at ordinary pressures in the presence of adequate oxygen, for it is fatal in concentrations of 39 volumes per cent.

Recovery from gas anesthesia is very rapid; demonstrable traces are not present after five to ten minutes. This is on account of, first, the rapid excretion, not much anesthetic being stored in the blood and tissues because the solubility coefficient is low. Furthermore, the gas narcotics do not interfere with the efficiency of the circulation or the depth of the respiration; they find better transport facilities for their excretion than do narcotics which impede their own elimination by depressing respiration, circulation or both. The gas

anesthetics, while producing general depression of the central nervous system, exhibit a greater specificity for depression of sensation and consciousness than do ether and chloroform which, as already mentioned, are more prone to disturb the centers of respiration and circulation.

Since gas anesthetics are controlled more readily than ethyl ether and are more specific depressants of the central nervous system they are all essentially safer in the more serious conditions. In particular, severe major operations, shock, grave hemorrhage or sepsis, cardiac, respiratory and renal diseases and acidotic states are regarded as indications for gas anesthesia. Where myocardial involvement is definite it would appear that the order of safety is: nitrous oxide, ethylene, cyclopropane.

NITROUS OXIDE

Paul Bert believed that one atmosphere of nitrous oxide suffices to produce deep narcosis even when an atmospheric quota of oxygen is coincidently introduced under pressure. Brown, Lucas and Henderson have definitely demonstrated that this is not the case, and that without anoxemia even 174 volumes per cent nitrous oxide are insufficient to produce deep narcosis. Two atmospheres of nitrous oxide are necessary to anesthetize completely in the presence of adequate oxygen, and three atmospheres to produce death under the same conditions. Ninety-five per cent nitrous oxide potentiated by partial asphyxia (5 per cent oxygen) suffices to produce complete anesthesia in the absence of other medication.

Ninety-five per cent of nitrous oxide plus 5 per cent of oxygen gives a shorter period of anesthetic induction in the rat in the presence of morphine than without it (Barlow and Stormont). This drug also lengthens the duration of the anesthesia even when the N_2O is lowered to 85 per cent. Fifteen per cent of the minimal lethal dose of morphine sufficed to maintain nitrous oxide anesthesia for at least thirty minutes in the absence of anoxemia.

Nitrous oxide exerts no irritation or toxic action upon the lungs, heart, kidneys or brain. Its inhalation in pure form results in the loss of consciousness after a few breaths, consciousness returning within thirty seconds. The skin assumes a dull pink color but as soon as asphyxia is allowed to appear the deep blue of cyanosis is evident. Postanesthetic vomiting is rare.

Even when given with oxygen and excess pressure, nitrous oxide does not produce complete muscular relaxation. When acidosis, hyperglycemia, dyspnea or circulatory depression occur they are always attributable to anoxemia rather than to the gas. As mentioned under the ether discussion, when that anesthetic is combined in any percentage with nitrous oxide the pharmacological results have been shown to be directly additive.

Under nitrous oxide respiration at first is slow, shallow and irregular. Indications of delirium may occur. The muscles are somewhat spastic, usually with slight limb movements, but definite excitement does not occur in the absence of excessive oxygen. The eyeballs wander and the pupils are dilated and react to light; the other eye reflexes are present. In surgical anesthesia under nitrous oxide and oxygen the respiratory rate is from twenty to thirty per minute. As with ether, the eyeballs eventually become fixed and the pupils smaller with a loss of the conjunctival reflex and then the corneal reflex. The circulation remains unchanged. Under still deeper anesthesia, involving a considerable degree of anoxemia, muscular relaxation does not improve but indications of collapse may appear. Unless the oxygen supply is increased clonic spasms analogous to asphyxial convulsions may develop.

The addition of ether or the complete change to ether anesthesia usually relieves the difficulties of nitrous oxide anesthesia. Pure oxygen must always be given when doubt is present as to the depth of the narcosis.

Toxic impurities which may occur in nitrous oxide include especially the higher oxides of nitrogen.

ETHYLENE

W. E. Brown, and independently, Luckhardt and Carter showed that ethylene is a direct depressant of the central nervous system in concentrations of 90 volumes per cent with oxygen 10 per cent. The motor reflexes are abolished and some of the phenomena produced are asphyxial but these can be overcome by the addition of oxygen. Surgical anesthesia is easily produced by ethylene and the effects of ethylene-oxygen anesthesia scarcely differ from those described for nitrous oxide-oxygen. As the table shows, the solubility coefficient in blood is less than that of nitrous oxide; hence ethylene is more rapid in action. It differs also from nitrous oxide in its capacity to cause a greater muscular relaxation which, however, is less complete than that produced by ethyl ether. Miller and Plant found the gastrointestinal musculature stimulated rather than depressed.

Ethylene produces neither respiratory irritation, salivary stimulation nor sweating. Recovery is rapid and postoperative nausea rare. The skin should be pink throughout the narcosis but if anoxemia becomes too marked an ashen gray cyanosis develops. The red blood cells are increased in number, as with ether; their osmotic resistance is likewise decreased. Any metabolic changes are insignificant unless attributable to asphyxia.

Heat regulation is but little affected by ethylene, and the temperature fall is ascribed chiefly to muscular relaxation. Of all the inhalation anesthetics ethylene appears the freest from undesirable pharmacological actions. Its chief disadvantage lies in its explosive and inflammable character.

Acetylene (CH:CH) is a gas of similar character to ethylene, with higher boiling point (−84°c) and greater oil solubility. For many in Europe it has filled the place occupied by ethylene in this country. The potency of acetylene is greater than that of ethylene for which reason it can be administered at ordinary pressures with adequate oxygen. It has the capacity to raise the blood pressure.

CYCLOPROPANE

While investigating its isomer, propylene, Lucas and Henderson found cyclopropane to be more powerful and less toxic than that gas. As indicated by the table its solubility coefficient for blood is more than twice that of nitrous oxide; this means slower induction of anesthesia. While effective as an anesthetic in 13 volumes per cent concentration, after preliminary morphine injection, this concentration must be doubled to produce anesthesia independently. When the first mentioned concentration is trebled death ensues. Leake's "therapeutic ratio" for cyclopropane in mice is 2.0.

It has been found that the tissues fix 27.5 mg. per 100 grams of body. As this is about one-quarter of the fixation of ether a much more rapid induction of anesthesia takes place.

Because of the high oxygen concentration possible with this anesthetic it is apparently superior for many types of cases. It is non-irritating, except in high concentrations, and can be adequately given without depression of respiration or circulation. Cyclopropane does not appear to affect the metabolism or seriously to affect the liver. Romberger has described the following stages of anesthesia produced by cyclopropane: the induction stage, ending with the disappearance of the lid reflex; "moderate anesthesia" ending with the disappearance of the eyeball movements; deep anesthesia.

Anesthetists accustomed to observe respiratory augmentation by diaphragmatic breathing with other anesthetics may be misled by its absence with cyclopropane. The breathing bag should be watched to avoid entering upon the stage of respiratory depression. Laryngospasm occurs only at high concentration.

Waters finds that the most valuable signs warning that the limit of tolerance has been reached are changes in the character of the pulse. Arrhythmia, slowing of the rate to 50 and less, or a definite increase in rate demands a reduction in gas con-

centration by the addition of a considerable quantity of oxygen. Color cannot be used as an indication of the degree of narcosis, and Waters believes that carbon dioxide is contraindicated.

Electrocardiographic studies sometimes indicate an increase in the irritability of the heart; while this is slight it must be kept in mind. Recovery appears to be accompanied more frequently by nausea than is the case with nitrous oxide or ethylene. Wood finds that cyclopropane may be combined to advantage with tribromethanol but not when disease of the liver or kidneys is present. The disadvantages of cyclopropane are its inflammability and explosibility as well as its marked potency at atmospheric pressure.

SUMMARY

The chief pharmacological effects of ethyl and vinyl ethers, chloroform, of the gas anesthetics in general and nitrous oxide, ethylene and cyclopropane in particular have been described. Most completely detailed are the effects of ether, the other anesthetics being discussed in part by comparison.

The conditions which control the absorption and fate of anesthetics, the methods of determining the factors of safety, the principles of preanesthetic medication and combination narcosis have all been pointed out, as well as the present status of the theory of narcosis.

Emphasis has been laid upon those features of anesthetic action which are of greatest clinical significance. The more important physical characters of the six anesthetics and their minimal anesthetic and lethal concentrations in the inspired air and the blood are presented in tabular form.

The appended bibliography affords a key to recent advances in the field of the inhalation anesthetics.

REFERENCES

General.

Henderson, Y. *Brit. Med. Jour.*, 2: 1170, 1925.

Kochmann. Handbuch der experimentelle Pharmakologie., Heffter-Heubner, Suppl. Vol. 2, pp. 1–110.

Narcosis Theories.

Henderson, V. E. *Physiol. Rev.*, 10: 171, 1930.

Meyer, K. H. and Gottlieb-Billroth, H. *Zeitschr. f. physiol. Chem.*, 112: 55, 1920.

Ethyl Ether.

Barbour, H. G. and Bourne, W. *Am. Jour. Physiol.*, 67: 399–410, 1924.

Bourne, W., *Jour. Pharmacol. and Exper. Therap.*, 28: 409–432, 1926.

Haggard, H. W. *Jour. Biol. Chem.*, 59: 737, 751, 771, 795, 1924.

Henderson, Y., Haggard, H. W. and Coburn, R. C. *J. A. M. A.*, 74: 783–786, 1920.

MacNider, Wm. deB. *Anesth. and Analg.*, 14: 97–101, 1935.

Peoples, S. A., Abreu, B. and Leake, C. D. *Jour. Pharmacol. and Exper. Therap.*, 57: 138, 1936.

Sheard, Charles, Rynearson, E. H. and Craig, W. McK. *Jour. Clin. Invest.*, 11: 183–193, 1932.

Vinyl Ether.

Bourne, W. and Raginsky, B. B. *Brit. Jour. Anesth.*, 12: 62, 1935.

Goldschmidt, S., et al. *J. A. M. A.*, 102: 21, 1934.

Leake, C. D., Knoefel, P. K. and Guedel, A. E. *Jour. Pharmacol. and Exper. Therap.*, 47: 5, 1933.

Chloroform.

Buckmaster, G. A. and Gardner, J. A. *Proc. Roy. Soc. Med.*, 79: 555, 579, 1907.

Cushny, A. R. Pharmacology and Therapeutics, xi ed., Revised by Edmunds & Gunn, Phila., 1936, p. 334.

Rosenfeld, Max. *Arch. f. exper. Path. u. Pharmakol.* 37: 52, 1896.

Nitrous Oxide.

Barlow, O. W. and Stormont, M. F. *Jour. Pharmacol. and Exper. Therap.*, 46: 141, 1932.

Brown, W. E., Lucas, G. H. W. and Henderson, V. E. *Jour. Pharmacol. and Exper. Therap.*, 31: 269, 1927.

Greene, Charles W. and Currey, Hiram M. *Arch. Int. Med.*, 35: 371, 1925.

Lendle, L. *Arch. f. exp. Path. u. Pharmakol.*, 146: 167, 1929.

Ethylene.

Brown, W. E. *Can. Med. Assn. Jour.*, 13: 210, 1923.

Halsey, J. T., Reynolds, C. and Prout, W. A. *Jour. Pharmacol. and Exper. Therap.*, 26: 479, 1926.

Luckhardt, A. B. and Carter, J. B. *J. A. M. A.*, 80: 765, 1923.

Miller, G. H. and Plant, O. H. *Jour. Pharmacol. and Exper. Therap.*, 25: 147, 1925.

Cyclopropane.

Kurtz, C. M., Bennett, J. H. and Shapiro, H. H *J. A. M. A.*, 106: 434, 1936.

Lucas, G. H. W. and Henderson, V. E. *Can. Med. Assn. Jour.*, 21: 173, 1929.

Romberger, F. T. *Anesth. and Analg.*, 14: 65, 1935.

Seevers, M. H., Meek, W. J., Rovenstine, E. A. and Stiles, J. A. *Jour. Pharmacol. and Exper. Therap.*, 51: 1, 1934.

Waters, R. M. and Schmidt, E. R. *J. A. M. A.*, 103: 975, 1934.

Wood, Paul M. *J. A. M. A.*, 106: 275, 1936.

PRESENT STATUS OF INHALATION ANESTHESIA*

RALPH M. WATERS, M.D.

MADISON, WISCONSIN

A CONSIDERATION of the "present status" of any branch of science must be concerned with the extent to which the fundamental problems of the field have been satisfactorily solved. The basic problem of anesthesia is the provision of pain relief under ideal circumstances and with a perfect agent and technique. The particular properties which this drug and technique should possess hardly need restating here. Many years ago the requirements of anesthesia were simple and premature. The production of pain relief while surgical manipulation was carried out was then almost the only desideratum. Today, the great advances in surgical technique, the more ambitious nature of the surgery attempted, and the greatly augmented critical attitude of the surgical profession have introduced many new conditions as requirements of good anesthesia. Much has been said regarding the relative merits of various agents and techniques now available, and the trends in their choice for inhalation anesthesia and what they offer, will be presented.

If one were influenced only by the nature and content of the articles currently appearing in the surgical journals, he might be forced to conclude either that inhalation anesthesia has been perfected and hence there is no more to write about it, or that it has been discarded completely. The articles concerned with drugs intended to produce pain relief describe their introduction into the body by way of the veins, tissues and rectum, or by any route other than through the pulmonary alveoli. These non-volatile agents are always compared to the use of ethyl ether spilled in a haphazard manner on a gauze mask. The convenience to the surgeon in quick induction, banishment of the anesthetist from the region of the face, quick and pleasant recovery for the patient and many other advantages are emphasized. When a "poor guess" as to dosage, or technical fault results in failure from the use of non-volatile agents, the habit seems to be to resort to "open" ether. The contrast is strikingly favorable, of course, to the non-volatile agents. A patient frightened by a therapeutic failure is scarcely a good subject for the beginning of another technique, even if the one chosen represented the best that there is to offer.

The belief in some quarters in the past that the administration of a drug by inhalation is a simple procedure which can be safely accomplished by the youngest and least experienced physician available, or even by a non-medical technician, was unfortunate. During the last quarter of a century we have come to realize that a method of drug administration which has remained effective and in the main safe when relegated to the hands of the inexperienced or even of the ignorant, must be possessed of possibilities for the greatest safety and perfection if placed in the hands of skilled and capable physicians. Drugs, whether injected or inhaled, which produce complete abolition of the effect of sensory stimuli are accompanied by more or less depression of physiologic processes, particularly the function of respiration. There is no injection drug, be it a derivative of barbituric acid, of alcohol, of opium, or of any other origin, including locally acting agents, which, in completely effective doses, does not sometimes approach a dangerous disturbance of respiration and other vital functions. At best, non-volatile agents when injected must be given in pre-

* From the Department of Anesthesia, Medical School, University of Wisconsin.

determined and to a certain extent "guessed" dosage. No two individuals receive exactly similar sensory depression from similar doses of any drug, whether calculated by weight, by age, or in any other way. Obviously, the shortest acting non-volatile agent will, other things being equal, prove safest. Even with the most rapidly destroyed agents suggested for anesthesia by injection, the recovering of depression is relatively slow as compared with volatile or gaseous agents.

Inhalation agents are now available which will induce sleep with no more unpleasant sensation than that involved in tolerating facial contact of a covering for the nose and mouth. Techniques are in extensive use which will assure complete control of the patient's respiration and anesthetic concentration with the anesthetist at the foot of the table if necessary. Closed endotracheal airways[1] will even permit the surgeon to irrigate thoroughly the nasal sinuses and the whole upper respiratory tract without danger of contamination of the lungs or interference with normal pulmonary ventilation. Artificial respiration with oxygen is available at all times. At the same time, advances in physiology have taught us how to balance and stabilize the disturbances accompanying the inhalation of drugs for pain relief.

This better physiologic understanding has been found useful or even life-saving in the correction and control of disturbances accompanying the injections of non-volatile anesthetic drugs. The introduction of agents through the respiratory tract is technically no more difficult than the essential control of oxygen and carbon dioxide tension of the inspired air which is an admitted accessory to injection anesthesia. To one who for many years has been concerned with the study of anesthetic drugs, non-volatile by injection and volatile or gaseous by inhalation, both in the laboratory and in the operating room, a greater feeling of safety and control, of having both the wheel and the throttle in one's hands, is experienced when the major portion of sensory depression is being produced by drugs which enter and leave the patient's circulation under second to second control through the alveoli.

DRUGS

Roughly, there are eight drugs now available for the production of anesthesia by inhalation. Four of these were tried before 1850; namely, nitrous oxide, ethyl ether, chloroform, and ethyl chloride or other hydrocarbon radical haloids. The other four, ethylene, acetylene, vinyl ether and cyclopropane have become popular since the Great War. In the first decades of surgical anesthesia, no thought was given to the need of administering anesthetic agents in an oxygen enriched atmosphere. With this addition, Wells might have had better success with nitrous oxide. We now know that chloroform administered in an oxygen atmosphere may cause as little liver necrosis as ether in air, and that ether administered in an oxygen depleted atmosphere may cause more liver necrosis than chloroform in air.[2] Possibly, improved methods of administering these older agents is the path along which future perfection may lie. Meanwhile, one is tempted to feel that a distinct contribution has been made in one or more of the four agents introduced in recent years. The attempt to find a new volatile liquid has continued throughout almost a century since Simpson's suggestion of chloroform as a substitute for ether.

Vinyl ether is the only suggestion of a new volatile liquid which has reached the stage of extended clinical trial[3] and many have preferred it to ethyl ether. In our hands, it has produced unconsciousness slightly more rapidly and comfortably, but the character of the resulting surgical anesthesia has not been comparable to that of ethyl ether. Reports of satisfactory results with this agent seem to have issued from cities at sea level, whereas those using the drug at higher elevations are less enthusiastic. Detailed knowledge of possible pathologic and pharmacologic damage is lacking still.

GASES

During a hundred and thirty-six years since the suggestion of Davy that nitrous oxide might relieve the pain of surgery, this drug has remained the only agent not a hydrocarbon. It has maintained a universal reputation for usefulness. Its only handicap has been lack of potency unless administered in an atmosphere of extremely low oxygen tension. All attempts to discover a gas with greater potency have necessitated resort to members of the hydrocarbon series, unsaturated hydrocarbons with one exception, and all retaining the fire hazard characteristic of the ethers. The introduction of a halogen atom in any hydrocarbon gas to eliminate or reduce the fire hazard has not been successful. At best, halogen compounds as anesthetic agents so far have proved unnecessarily toxic to parenchymatous tissue. Until a gas is discovered with the innocuous properties of nitrous oxide, but with such potency as to assure deep surgical anesthesia without the danger of oxygen want, the interest of anesthetists in gaseous hydrocarbons is justified.

Ethylene and acetylene, two simple unsaturated hydrocarbons, possessing in the case of the latter at least, distinctly greater potency than nitrous oxide, have for several years held the field. The suggestion of Henderson and Lucas[4] in 1929 that cyclopropane, a saturated hydrocarbon gas with a ring structure, might serve the purpose of anesthesia, has occupied the more recent attention of practical and experimental anesthetists. Numerous reports from the University of Wisconsin and a greater number from other sources offer incomplete testimony on which to base judgement of the suitability of this agent for clinical anesthesia. Suffice it to say here that our investigations have seemed to justify the continued use of cyclopropane to such an extent that 55 per cent, or 5889 administrations, of the inhalation anesthesia at the Wisconsin General Hospital in the three year period 1933, 1934 and 1935 utilized this agent. The comparative postanesthesia and postoperative respiratory morbidity has been distinctly less[5] and the circulatory morbidity more, than following other inhalation agents.[6] Further studies of the mechanism of circulatory changes accompanying the inhalation of cyclopropane are being continued with the object of determining their significance. Pleasant induction of unconsciousness and unlimited depth of anesthesia without oxygen want characterize this agent to a degree not seen with other agents now in use.

METHODS

Speed and ease of control of the tension of anesthetic gas or vapor in the alveoli are essential to good inhalation anesthesia. Similar control of the concentration of oxygen and carbon dioxide is necessary if disturbance of physiologic activity is to be avoided. The control of the latter factors is quite as important following the injection of non-volatile agents as it is during inhalation anesthesia. Developments of the past twenty-five years have made available pharyngeal and endotracheal airways which assure free breathing and protection from pulmonary flooding with blood and other foreign matter, whatever the demands of surgery. By means of the chemical absorption of carbon dioxide from respiratory atmospheres, a completely closed system is available assuring a warm, moist, nonirritative atmosphere under second to second control as to its content of oxygen and carbon dioxide as well as the tension of anesthetic gas or vapor.[7]

CONCLUSIONS

For safe anesthesia, the need for constant supervision of respiration, with occasional assumption of active control, will always require the presence of a physician familiar with the signs of carbon dioxide and oxygen imbalance as well as with the pharmacologic effects of the various agents. Such an individual, to be completely safe, must be expert in the insertion

of airways and control of the respired gases. These are essential requirements for the patient's safety whether drugs are administered by injection or by inhalation.

It is our sincere belief that the knowledge and application of well planned physiologic principles to the technique of anesthetic administration is the all important factor in safe and pleasant results, not the particular drug that may be chosen. The correction of faulty carbon dioxide-oxygen balance in the patient's tissues, avoidance of cold and irritating atmospheres in the respiratory tract, maintenance of a free airway at all times, fortification and control of the fluid and salt balance, are the factors which determine our results whatever drug or method may be selected.

REFERENCES

1. Guedel, A. E. and Waters, R. M. Endotracheal anesthesia: a new technic. *Ann. Otol., Rhinol. and Laryngol.*, 40: 1139 (Dec.) 1931.
2. Ravdin, I. S. Personal communication.
3. Goldschmidt, S., Ravdin, I. S., Muller, G. P., Johnston, C. G. and Ruigh, W. L. Divinyl ether: experimental and clinical studies. *J. A. M. A.*, 102: 21–27 (Jan. 6) 1934.
4. Henderson, V. E. and Lucas, G. H. W. A new anesthetic gas: cyclopropane. *Can. Med. Assn. Jour.*, 21: 173–175 (July), 1929.
5. Rovenstine, E. A. and Taylor, I. B. Postoperative respiratory complications: occurrence following 7874 anesthesias. *Am. Jour. Med. Sc.*, 191: 807 (June) 1936.
6. Schmidt, E. R. and Waters, R. M. Cyclopropane anesthesia: postoperative morbidity in 2200 cases. *Anestb. and Analg.*, 14: 1–3 (Jan.-Feb.) 1935.
7. Waters, R. M. Carbon dioxide absorption from anesthetic mixtures. *California and West Med.*, 35: 342 (Nov.) 1931.

ENDOTRACHEAL ANESTHESIA

I. W. MAGILL, M.B., D.A.

Senior Anesthetist Westminster and Brompton Chest Hospitals, London

LONDON, ENGLAND

THE maintenance of a free airway has long been recognized as a first principle in general anesthesia and the danger of complete laryngeal obstruction has always been obvious. On the other hand the cumulative effects of partial respiratory obstruction have, in the past, been frequently overlooked and it is not improbable that many of the surgical difficulties, postoperative complications, and even fatalities attributed to the anesthetic agent have been primarily due to an imperfect airway. It may be said without exaggeration that in remedying this defect endotracheal anesthesia has proved as great a factor in the advances of anesthesia as the discovery of new drugs or the development of improved apparatus. Thus, apart from the advantages it offers to the surgeon, the safeguard afforded to the patient may prove to be a definite factor in the reduction of the deaths and complications for which general anesthesia has been held responsible. Historically, laryngeal intubation is older than general anesthesia. It has been clearly shown by Waters, in his comprehensive account of the development of endotracheal methods, that many devices and points of technique which have been described as new in recent years had already been discovered by former observers.

Although Kuhn was the first to recognize the value of intubation anesthesia, through the nose as well as the mouth, it would appear that the chief stimulus to modern development in endotracheal anesthesia was due to Elsberg, who applied to the human subject the insufflation principles which Meltzer and Auer had demonstrated with such success in animals. Here, the possibility of safely opening both pleural cavities with the insufflation technique eclipsed many advantages of intubation as we know them to-day. Development improved with the opportunities given by the Great War. In England, the segregation of facial and jaw injuries in a special hospital at Sidcup devoted to reconstructive surgery called for special skill when general anesthesia was required, and in time endotracheal anesthesia became the routine method. It was not long before its advantages in plastic surgery were widely recognised, and its use has since been rapidly extended to other surgical fields.

So much is this so, that, owing to the ease of control it affords, there is a tendency towards its employment in every operation, regardless of other considerations. This tendency is to be deprecated, especially in the teaching of students. The novice should learn airway control by simple methods in the first instance, for he may be called to administer an anesthetic in circumstances in which artificial devices are not available. Moreover, as the method involves instrumentation, which is not devoid of the risk of trauma, even though it may be slight, intubation should only be attempted when the necessity for it has been considered carefully.

USE OF ENDOTRACHEAL ANESTHESIA

Advantages.

1. In most circumstances the anesthetist has complete control of the airway.
2. There is no tax on the respiratory mechanism of the patient.
3. Respiration being under control and unhampered, it is possible for light and even anesthesia to be maintained.
4. The patient can be protected against the entry of blood into the trachea.
5. The anesthetist and his apparatus are clear of the field of operation.

6. The surgeon is protected from the patient's exhalations, an important factor in oral operations.

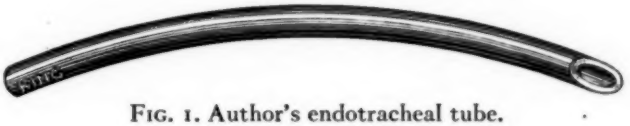


Fig. 1. Author's endotracheal tube.

7. Endotracheal or endobronchial suction can be employed in certain thoracic operations without interference with the anesthesia.

8. The anesthetic can be confined to one lung, leaving the other in a state of collapse.

Disadvantages.

1. The service of an anesthetist skilled in intubation is essential.

2. Instrumentation is required, carrying with it the risk of trauma, usually in the form of postoperative sore throat.

3. In pharyngeal operations the endotracheal tube occasionally may encroach on the surgical field.

Indications.

1. Operations upon the head and neck, with the exception of those involving the vocal cords;

2. Operations in which the type of patient, his position on the table, or the nature of the surgical procedure may cause difficulties in the control of the airway;

3. Certain thoracic operations when performed under general anesthesia.

Contraindications.

1. Acute mastoiditis (owing to the danger of spreading infection in the air passages);

2. Acute inflammatory disease or new growth close to the vocal cords;

3. Operations for toxic goitre, except when the pressure on the trachea causes gross respiratory embarassment;

4. Thoracoplasty.

EQUIPMENT

A direct vision laryngoscope is an essential part of the anesthetist's outfit. Any good instrument will suffice, but illumination from a self-contained battery is a convenience. The slot in the barrel should be wide enough to accommodate large tubes. This facilitates withdrawal of the laryngoscope when the tube has been passed by the mouth.

Endotracheal catheters (Fig. 1) may be made of flexible metal tubing, rubber covered metal spring coils, gum elastic, or mineralized rubber. Rubber is preferable to any other material for intranasal intubation, and for routine work the mineralized variety has much to commend it. This material is comparatively innocuous when in contact with mucous membranes, combines flexibility with resilience, is easily sterilized and is cheap; moreover rubber tubing, being stored in coils, has a natural curve which is readily adaptable to the course of the air passage from the nose or mouth to the glottis.

Size of Tube. The rubber endotracheal tubes are bevelled at the end and are carefully smoothed off with a carborundum stone or an emery nail file. Twelve sizes are obtainable, and afford a comprehensive range for patients of all ages and different physiques. Recently the makers have moulded these tubes individually instead of cutting them from a coil. Sizes 4 ($^{17}/_{64}$ inch) to 8 ($^{21}/_{64}$ inch) are made in two thicknesses; the thick walled tubes are used for oral intubation and the thin walled variety are passed through the nose. In the smaller sizes this differentiation is unnecessary.

Correct Length. A ready measure is twice the distance between the lobe of the ear and the ala of the nose. It is important that the length should be suited to the individual. The end of a tube that is too short may rest near the glottis without passing through it, and may become obstructed from time to time, while a tube that is too long may pass into one or other bronchus. The latter is most likely to occur in children. The calibre of the tube to be chosen depends upon the physique of the patient rather than on his age. The tube selected should be the largest which the

larynx will accommodate without injury; No. 8 is the most useful for adults, but great care is required in the choice of the

FIG. 2.

FIG. 2. The tube-to-apparatus connections.

correct size for infants and young children. In all cases the tube should be large enough to permit free to-and-fro respiration through its lumen.

Care of Tube. It is essential to remember that rubber is affected by climate, age, use, disuse and abuse. Therefore the anesthetist must be sure that the tubes are in good condition. If they have been unused for a time they tend to become hard, but kneading and gentle heat will often restore them to condition. Prolonged boiling causes the rubber to become soft and useless. In no case should the tube be boiled for any length of time with a metal connection attached to it. Its shape is retained best when circular boxes are used for storage.

Since trauma is the chief disadvantage of intubation, it is clear that the keynote of success lies in careful attention to details of technique. It is practically impossible for the anesthetist to be aseptic, but a combination of ordinary cleanliness with the use of suitable antiseptics compensates for this defect. Thus, particular attention should be paid to the state of the tubes, both inside and out. When the responsibility rests with a nurse it is not unusual to find the inside of the tube neglected. The small brushes used for bronchoscopes are useful for cleaning purposes. The tubes should be boiled for two minutes before use and immersed in 1:1000 biniodide of mercury until they are required. They should then be carefully lubricated with sterile soft paraffin.

Metal Connections. When it is intended, as is usually the case, to connect the tube to an anesthetic machine, a set of angular metal connections are required. (Fig. 2.) The wide angled type is chosen for oral intubation, in which case the anesthetic apparatus is at one side of the operating table. The acute angled connections are intended for use when the tube is passed through the nose and the anesthetic apparatus is placed at the head of the table.

TECHNIQUE OF INTUBATION

1. Preliminary cocainization of the upper air passages has proved advantageous in the writer's experience. This is accomplished by means of a small quantity of 20 per cent solution with a few drops of adrephine added, delivered from a fine spray. The advantages of cocainization are that (*a*) intubation can be done without recourse to deep anesthesia; (*b*) in nasal intubation maximum patency of the passage is assured, and (*c*) the tube is tolerated without any coughing under light anesthesia. Cocainization is, however, open to objection on the grounds of (*a*) toxicity, although in the writer's experience no cause for anxiety has arisen, and (*b*) abolition of the cough reflex. This is protective and in its absence there is danger unless positive endotracheal pressure exists, or unless suitable packing or a Guedal-Waters inflatable cuff is used. In cases of regurgitant vomiting a stomach tube should be passed at the same time.

2. Protection of mucous membranes. Preliminary medication and dry anesthetic gases tend to dessicate the mucous membranes and render them more liable to injury by the laryngoscope, the throat packs or endotracheal tubes. This can be largely prevented by lubrication with sterile liquid paraffin, which also facilitates the introduction of the tube, especially when the nasal route is chosen. When using the laryngoscope the teeth should be protected by a piece of adhesive plaster.

3. Position of the patient's head. This is of the greatest importance, the correct position being the same whether intubation is done through the nose or through the mouth. Hyperextension, as for bronchoscopy, is not only unnecessary in most cases, but actually increases the difficulties of

intubation. The head should have the same relationship to the neck and trunk in the recumbent as in the erect position, and a pillow may therefore have to be placed below the occiput. The correct position on the table is that in which the cervical vertebras are in normal relationships to the dorsal and *are not extended*. The head itself is slightly extended on the atlas, so that the mandible is approximately at right angles to the table. When he wishes to sniff the air a man in the normal erect posture instinctively and unconsciously takes this attitude, throwing his chin slightly upwards, and leaves the natural air passage from nose to glottis as free as possible. When a mesial section is taken through the head and neck in this position, it is clear that the course of the air passage from nostril to glottis is curved. Consequently a rubber tube with a similar curve, introduced through the nose (or a catheter mounted on a curved stilette) can be made to follow that course quite naturally, and in a large percentage of cases will enter the glottis in preference to the esophagus.

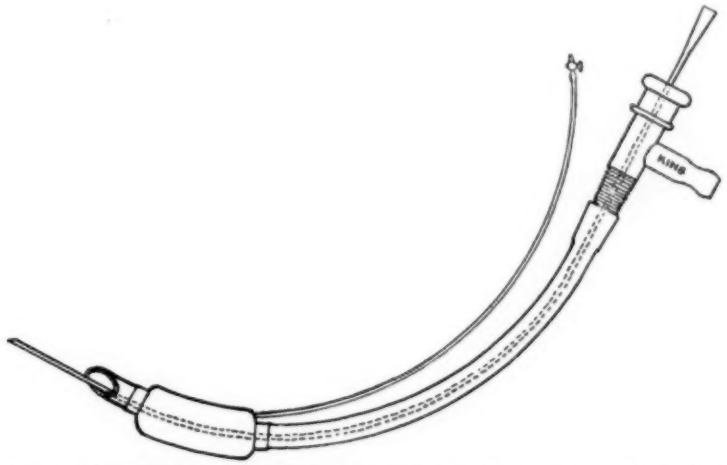


Fig. 3. Modified Guedel-Waters apparatus with endotracheal suction catheter.

NASAL OR ORAL INTUBATION?

Intubation can be performed either through the mouth or through the nose. The relative advantages of intranasal intubation are considerable as compared with the oral method. The nasal technique may be carried out under light anesthesia* without muscular relaxation, and there is no risk of damage to the teeth or to growths which would be in danger from the laryngoscope which is required for the oral method. It is further of great value in intra-oral operations, and, being easy to perform, is the first choice when no contraindications exist. It is not intended to enumerate in detail the technique for the oral method. For a detailed description readers are referred to Chevalier Jackson's Bronchoscopy, Esphagoscopy and Gastroscopy.

"BLIND (NASAL) INTUBATION," AUTHOR'S TECHNIQUE[1]

To be successful with this method free nasal breathing should be possible on at least one side, and where a difference exists the side which is most patent should be chosen. This should be ascertained before induction. The tube is passed along the floor of the nose close to the septum. When a point is reached at which the respiratory sounds are heard at the maximum intensity the tube will then enter the glottis when it is pushed onwards during inspiration. The administration of a small quantity of CO_2 is a useful adjunct at this point as it

* The special advantage here is that the tonus of the jaw muscles actually draws the epiglottis away from the posterior pharyngeal wall.

[1] See *Proc. Roy. Soc. Med.*, Section of Anaesthetics. 22:4 (Dec.) 1928.

brings about a wide separation of the vocal cords. In the case of failure, the tube should be rotated to one side or the other in order to bring the tube into the desired position. Occasionally gentle manipulation of the larynx with the left hand may be required in addition. In some instances where the epiglottis is the obstacle the difficulty can be overcome by withdrawing the tube one inch and rotating it so that the convexity is anterior. If pushed onwards in this position the end of the tube will frequently pass behind the epiglottis and when it is again rotated into the original position the free end will enter the larynx. To be sure that the tube is not coiled up in the pharynx or in the esophagus breath sounds should be listened for at the outer end. In the event of failure to insert the tube properly they will be inaudible. In difficult cases it will be necessary to use a laryngoscope, and so pass the tube, grasped in suitable forceps, directly into the glottis.

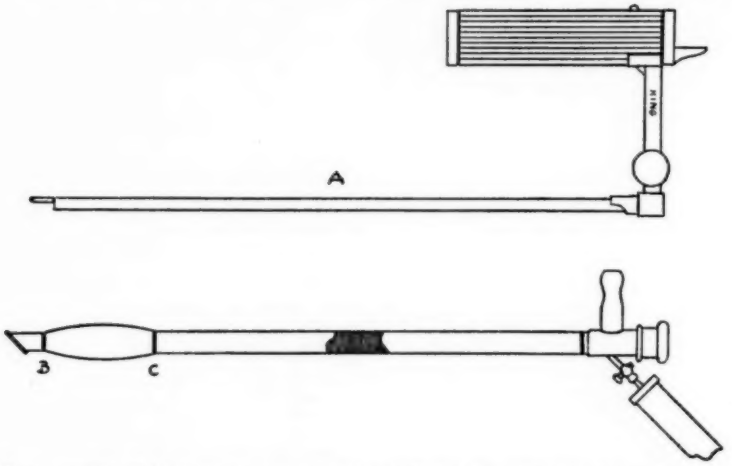


Fig. 4. Flexible bronchoscope with inflatable cuff for "one lung" anesthesia.

Maintenance of Anesthesia

Anesthesia can be maintained on ordinary inhalation principles and the system may be opened or closed. For closed anesthesia the Guedel-Waters inflatable cuff is invaluable, but cannot, of course, be passed through the nose without risk of trauma. Any efficient gas-oxygen apparatus may be used to maintain anesthesia and to apply positive pressure should this be desired.

Gauze packing, boiled with soft paraffin, may be used to ensure that breathing takes place through the tube and not outside of it. In mouth operations this also prevents blood from reaching the trachea. If carefully placed around the tube in the pharynx this packing is sufficient for practical purposes. In operations on the nose the gauze keeps the soft palate in apposition to the posterior wall of the pharynx. This method is more effective than the use of gauze or sponges in the post-nasal space, and is less likely to cause discomfort after the operation.

Special Application to Thoracic Surgery

The writer has already described[2] some features of this procedure. It is obvious that during an extensive intrathoracic operation, intubation is of the greatest importance owing to the danger of laryngeal spasm. Again, abundant secretion in the respiratory tract may result in two special difficulties; (1) at times secretions may almost completely block the air passage, and (2) they may spread to another lobe on the affected side or to the opposite lung, resulting in the atelectasis or subsequent pneumonia. Lobectomy and pneumonectomy for bronchiectasis present a problem which does not arise when the operation is undertaken for new growth,

[2] *Proc. Roy. Soc. Med.*, 29: 7–16 (April) 1936.

and consequently there have been certain developments in intubation technique.

There are three methods of intubation which meet the difficulties mentioned:

1. A rubber tube is passed in the usual manner. A catheter is then introduced into the trachea or bronchus on the affected side and left *in situ*, suction being applied when necessary. An inflatable cuff can be employed on the anesthetic tube and the catheter can be passed through the lumen of the tube. (Fig. 3.)

2. The second method requires the passage of a tube into the bronchus on the sound side, a rubber balloon being inflated at the bifurcation of the trachea, Water's technique. The instrument shown in Figure 4 is, however, used by the writer in the application of Water's method. A stiff inner canula, *A*, illuminated from a battery in the handle is passed into a metal tube consisting of a spiral of small bore tubing starting at the proximal end with a tap and finishing distally inside the inflatable cuff. This tube is covered by a close fitting rubber sheath tied securely in position with silk in three places. The cuff, *B*, *C*, is seen in the figure.

3. The third method entails the use of an endotracheal tube for the anesthesia, and the insertion into the bronchus on the affected side of a suction catheter carrying a balloon to close off the main bronchus. Reference to the figure (Fig. 5) will show that the anesthetic tube, *B*, held in its carrier, *A*, is used as a tracheoscope for the accurate insertion of the balloon-bearing catheter into the bronchus.

The effective application of any of these methods depends on the dexterity of the anesthetist and to some extent on the age and physique of the patient.

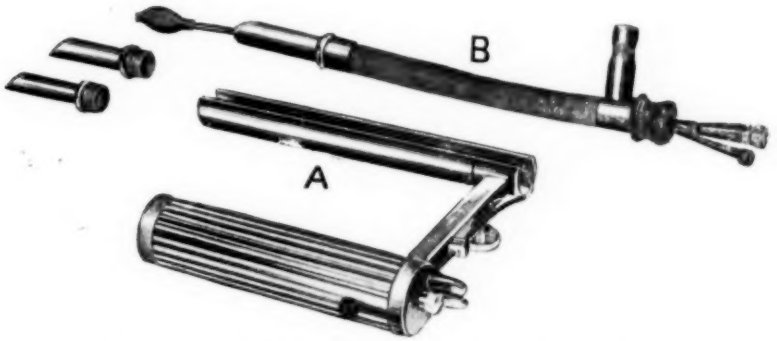


Fig. 5. Combined tracheoscope and anesthetic tube.

Method 1 may be used with patients of any age, but the inflatable cuff is impracticable with very young children.

Method 2 is particularly suited for pneumonectomy.

Method 3 is preferable for lobectomy, as suction can be maintained without interfering with the anesthesia. The affected lung is deflated and easy to handle, the small balloon prevents secretion reaching the trachea when suction is not being applied, and the flexibility of the rubber cap allows for movement of the catheter in accordance with the movement of the bronchus.

The majority of lobectomies are undertaken for lower lobe lesions, but there seems no reason why the balloon should not be placed distally to the origin of the upper lobe bronchus and so protect it and allow it to function during the operation.

I should like to acknowledge my indebtedness to Charles A. King, Ltd., London, for the blocks illustrating their instruments.

REFERENCES

Elsberg, Charles. *New York Med. Rec.* (March), 1910.

Jackson, Chevalier. Bronchoscopy, Esophagoscopy and Gastroscopy. Philadelphia and London, W. B. Saunders.

Magill, I. W. *Proc. Roy. Soc. Med.* (*Section of Anaesthesics*), 22:4 (Dec.) 1928; and 29: 7–16 (April) 1936.

Waters, Ralph M. Endotracheal anesthesia and its historical development. *Current Res. Anesth. and Anal.*, 12: 196–203 (Sept.-Oct.) 1933.

CARBON DIOXIDE ABSORPTION METHOD FOR INHALATION ANESTHESIA*

ITS DEVELOPMENT AND PRINCIPLES

E. A. ROVENSTINE, M.D.

Assistant Professor of Surgery, New York University College of Medicine; Director of Anesthesia, Bellevue Hospital

NEW YORK CITY

FUNDAMENTAL scientific discoveries that have paved the way for modern developments in the administration of inhalation anesthesia are innumerable. Servetus[1] described the lesser circulation of the blood nearly three centuries before surgical narcosis was realized. Harvey[2] announced the discovery of the circulation nearly a century later. In 1667 Hooke[3] performed experiments which showed that the essential feature of respiration was the blood changes in the lungs. Another century passed before Lavoisier[4] described the nature of the exchange of gases in the lungs and determined that an individual absorbs a definite amount of gas per hour depending upon his activity and the temperature of his environment. Mayon[5] gave the first account of oxygen a hundred years before Spallanzani[6] called attention to the fact that tissues consume oxygen and produce carbon dioxide. In 1757 Black[7] demonstrated that alkaline hydroxides absorb carbon dioxide. The inhalation of vapors and gases to produce surgical narcosis was not a reality until ninety years ago and the absorption of carbon dioxide from anesthetic mixtures has been practiced for less than a quarter of a century.

The basic chemical and physiological principles underlying the development of the carbon dioxide absorption technique for clinical anesthesia were utilized first for animal and human experimentation. Late in the eighteenth century Lavoisier and Priestley removed carbon dioxide and kept animals alive with constant additions of oxygen. The advent of submarine construction focused the attention of American investigators on similar experiments. In 1906 Brindley and Foregger[8] described experiments on the regeneration of air for submarines. They placed rabbits in a closed box with fused sodium peroxide to generate oxygen and absorb carbon dioxide. They found that in this manner animal life could be supported indefinitely. Shortly thereafter, the experiments were repeated with human subjects. The United States Government commissioned Brown[9] to complete the study and an experimental cabinet to simulate the conditions under investigation was constructed at Harvard University. Brown[9] and Foregger found that with the oxygen and carbon dioxide controlled, men were able to remain in this cabinet for many hours without untoward effects.

It remained for Jackson[10] to apply these facts to anesthesia and in 1915 he published a report of his use of the carbon dioxide filtration method for anesthetizing laboratory animals. He placed small animals in a closed box, added gas until narcosis was produced, provided a constant supply of oxygen and used caustic soda sticks for absorbing carbon dioxide. The animals remained anesthetized without further additions of the anesthetic agent. Waters observed the work done in Jackson's laboratory and was convinced the principle should be developed clinically since, as he stated, "the control of carbon dioxide elimination and oxygen intake is an essential corollary of all good anesthesia."[11] By persistent study, extensive clinical investigation, careful laboratory experimentation, development and improvement of appliances during the past twenty years,

* From the Department of Anesthesia, Division of Surgery, New York University College of Medicine.

Waters has established the method for controlling oxygen and carbon dioxide during the administration of inhalation anesthesia. Today every leading manufacturer of anesthesia appliances offers equipment for employing complete rebreathing and the absorption of carbon dioxide from anesthetic mixtures. The majority of physician anesthetists agree that there are definite advantages with the method and clinical anesthesia has made more progress since the inception of the technique than in any other period of like duration.

The revolutionary idea of complete rebreathing during the administration of inhalation anesthesia was not immediately accepted by the profession. The theoretical belief was current that expired air contained some poisonous volatile matter which had been termed "anthropotoxin." Many scientists including Haldane,[12] Yandell Henderson and Hill gave evidence against the theory. Lee,[13] as chairman of the New York Commission on Ventilation, finally disproved conclusively the presence of any such toxin. The role of carbon dioxide in respiration at the same time was being advanced rapidly by Haldane and Yandell Henderson. Gatch[14] in 1910, had applied their conclusion to rebreathing during anesthesia and designed an apparatus to utilize carbon dioxide. He maintained that excess carbon dioxide offered certain definite advantages over the commonly employed open techniques. The Boothby-Cotton[15] apparatus perfected about the same time favored the same principles. In 1915 there was no available apparatus that permitted a visible flow of gases with the essential accurate calibration to allow any desired rate of flow and no safe and efficient absorbing agent had been produced.

The demand for security against the effects of poisonous war gases resulted in the production of a practical carbon dioxide absorbing material. Wilson,[16] after experiments conducted for the United States Government adopted "Soda-Lime" for army purposes. This mixture of calcium and sodium hydrate had originated with Benedict[17] during nutritional experiments at the Carnegie Institute in Boston. Soda lime does not deliquesce on exposure to air and the chemical reaction with carbon dioxide produces no excessive temperatures. Extensive clinical observation and experiments have demonstrated the absence of any ill effects upon respiratory or other sensitive membranes and this has not been disproved conclusively in the laboratory. Although soda lime has proved efficient, it is readily agreed that there is need for improvement. An absorbing agent with less bulk, decreased generation of heat, absence of carbonate dust, and more capacity for absorbing carbon dioxide is desired.

Securing an apparatus suitable for the technique presented mechanical difficulties. In his early experiments Waters used the Gwathmey-Woolsey machine furnished by the Foregger Company but the absence of a fine control of the oxygen flow precluded successful results. It was not until 1922, that the same company furnished the original metric appliance with two water flow meters, one for nitrous oxide and the other for oxygen. In Germany, Dräger, in Lübeck, had used the "Kali-Patrone" or potash cartridge in rescue helmets before the war and for gas masks during the war. Shortly afterwards, he manufactured an anesthesia appliance employing this cartridge but its construction was such that the resistance to respiration precluded complete rebreathing. It was necessary to maintain a constant flow of the anesthetic gas as well as oxygen. Mechanical improvements have resulted from the past fifteen years experiments and today accurate and convenient flow meters for all the gases employed are assembled in compact units.

The construction of the closed respiratory system has followed two different lines of investigation. Waters first tried to adopt the principle of construction used in equipment for determining basal metabolism. This employed a circle device with one tube to carry the expired atmosphere to the absorber and another to return the carbon

dioxide deleted anesthetic mixture. He abandoned the circle absorber because of the difficulty in eliminating leaks, the

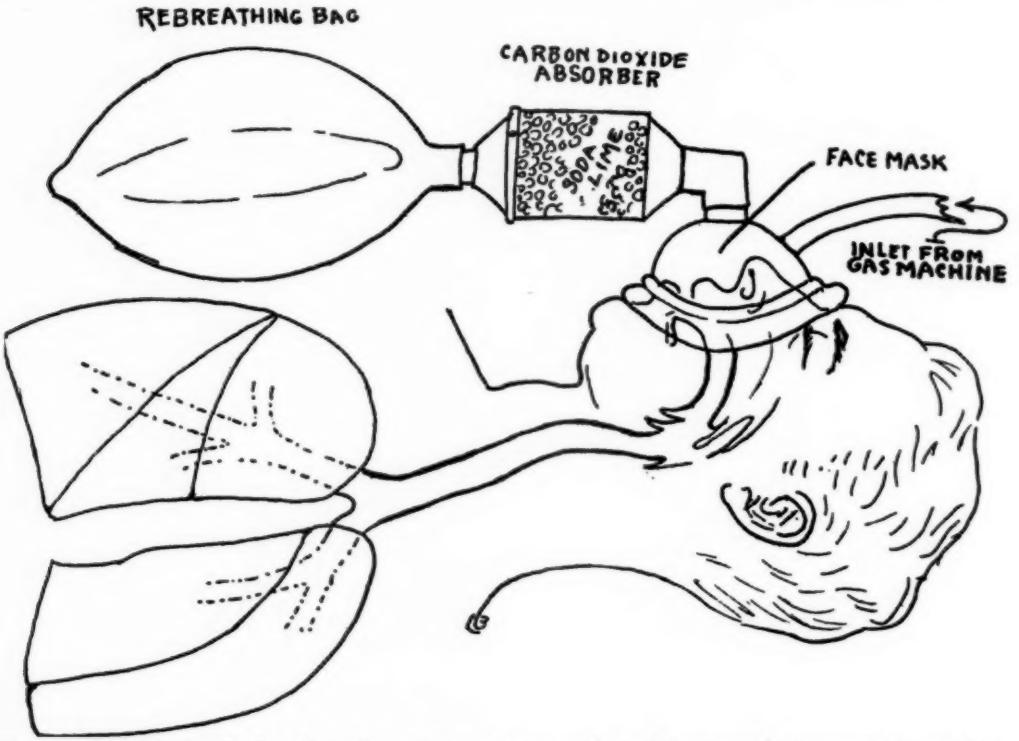


Fig. 1. Diagrammatic drawing of respiratory tract enlarged by anesthetic mask in airtight contact with face and the soda lime absorber and breathing bag.

resistance to respiration by forcing the atmosphere through tubing and one way valves and his reluctance to use any fan or pump to maintain circulation in the device without effort to the patient. Waters then devised the direct to and fro absorber which, as now used, consists of a cylindrical container for the absorbing agent. This canister is of proper dimensions that when filled with the correct size granules of soda lime, breathing through it may be accomplished without appreciable resistance. It is adjusted between the face mask and a small (5 liter) rebreathing bag by easily connected and leak proof metal slip joints. A hose nipple is provided on the face mask to introduce the anesthetic agent and oxygen from the machine.

In applying the principles of carbon dioxide absorption from anesthetic mixtures to practical operating room anesthesia, one merely enlarges the normal respiratory tract consisting of alveoli, bronchi, trachea, larynx, pharynx, mouth, nose and accessory sinuses to include a face mask, the canister for soda lime and a rebreathing bag; Figure 1 represents diagrammatically this enlarged respiratory tract. One needs, then, to make such an enlarged tract airtight, fill it with an anesthetic mixture suitable to produce the degree of narcosis desired for the patient, and provide a constant addition of oxygen just sufficient to adequately meet the metabolic requirements of the individual. It is claimed theoretically, that narcosis may then be indefinitely continued without further addition of the anesthetic agent since no change will take place in the concentration of the anesthetic gas or vapor once equilibrium with the blood is established. Practically, such ideal conditions are not always obtained.

Adjustments in the degree of narcosis desired for different operating conditions must be made with any technique. In protracted cases one seldom wishes to

maintain the same depth of anesthesia throughout the procedure. Frequent observations have made anesthetists cognizant of the fact that one-quarter hour of deep third plane anesthesia with complete muscular relaxation will do the patient more harm than two hours of second plane anesthesia. It is also true that an appreciable amount of the agent will be lost from the system. This varies with the drug used but in each instance there is a loss from the rubber breathing bag, from the skin surfaces and more especially from the operating wound. The amount of agent dissolved in the blood that is spilled is lost and there is a constant deletion directly from exposed tissues. Moreover, the saturation of blood by the anesthetic drug will take place rapidly and uniformly but saturation of the different tissues is not complete during the lengthiest operation. In ether anesthesia for example, Haggard[18] has shown that this rapidity of tissue distribution is proportional to the blood supply of the tissue. Saturation is rapid in the brain where the blood supply is great, but in fats where the blood supply is small the saturation is slow. It also follows that the metabolic requirements, or the tissue oxygen needs, are not absolutely constant during the different stages of narcosis and the oxygen flow once established may need be changed to prevent dilution or oversaturation of the anesthetic mixture. Such adjustments that need be made will depend upon the reflex obtundation necessary for the individual surgeon and must be individualized for each manipulation and every patient.

The employment of a completely closed system for protracted inhalation anesthesia introduced features not common with other techniques. (1) The patient breathes an atmosphere warmed with the heat generated by the chemical reaction between carbon dioxide and the alkaline soda lime; (2) this atmosphere is saturated with water vapor from his own exhalations; (3) the carbon dioxide and oxygen content of this atmosphere is accurately controllable by the anesthetist. It is upon these features and the advantages of convenience, improved surgical conditions, safety and economy that the merits of the method rest.

The aim of clinical anesthesia is to obtain obtundation of the patient's reflex irritability with minimal physiological disturbances. When attempting to achieve this ideal by inhalation methods one is constantly confronted with unphysiological disturbances of respiration. The control of normal respiration is accomplished by a normal functioning respiratory center, assisted by natural muscular activity and unhampered by obstructed airways. The anesthetist will, of necessity, invariably alter one or more of these regulating factors. Not the least disturbing is the attempt to maintain the respiratory center as it prevails in nature. This center is regulated by nervous stimuli from various sensory nerves of the body and more particularly, by the hydrogen ion concentration of the blood. This is represented by the ratio of carbonic acid (H_2CO_3) and sodium acid carbonate ($NaHCO_3$) or in the final analysis, the carbon dioxide content. The rate and depth of respirations are markedly changed by even slight variations of carbon dioxide. Increasing the carbon dioxide tension stimulates respirations and produces hyperpnea, while decreasing it slows respiration and produces apnea. It has been determined[19] that the stimulating effects are evident until concentrations in the inspired atmosphere of 30 per cent carbon dioxide are reached. These figures, however, are based upon normal individuals in a normal environment. In surgery, we do not usually have normal subjects. Rather, due to existing disease, the presence of hypnotic drugs and the changed environment, abnormalities are the rule. In the latter circumstance, the figures are extremely variable. Any increase in carbon dioxide inhaled may, under certain conditions, act as a respiratory depressant. The adjustments of oxygen, in addition to the regulation of carbon dioxide, so that

the nervous cells of the respiratory center may secure the considerable amount needed to satisfy their metabolic needs, is essential. Moreover, a reduction of the normal blood oxygen content produces rapid breathing and decreased carbon dioxide, apnea and finally failure of the respiratory center. This effect is likewise extremely variable and depends also upon the condition of the patient. A slight lack of oxygen may depress or a slight increase may stimulate the respiratory center of abnormal individuals. From the foregoing, it seems an obvious deduction that an accurate control of carbon dioxide elimination and oxygen intake is essential to inhalation anesthesia.

The carbon dioxide content of air is negligible, seldom exceeding .04 per cent. In normal individuals in normal atmospheres, the pulmonary alveolar concentration of carbon dioxide is 5 to 5.5 per cent and that of the expired air approximately 4 per cent. Haldane[20] has shown that increasing these percentages, even in normal subjects, has marked results. Continuous breathing of an atmosphere containing one per cent carbon dioxide will incapacitate men for work and 6 per cent will usually give subjective symptoms of malaise, headache, nausea and may even cause unconsciousness. Brown[9] found that the majority of men working in submarines were completely incapacitated when 6 per cent carbon dioxide concentrations of the inspired air were reached. He regarded it as the critical point. Granting that these results are obtained in normal individuals it must be evident that certain surgical patients might suffer more serious effects. The employment of the closed carbon dioxide absorption technique obviates such consequences. It is established that, while using the method the concentration of carbon dioxide in the inhaled atmosphere varies little from that of unanesthetized normal individuals. Active soda lime will absorb all the carbon dioxide in contact with it, but in the system a dead space exists in the pharynx, mouth and face mask (approximately 350 c.c. for adults) that retains carbon dioxide to maintain a normal physiological balance. Repeated analyses[21] have established an average concentration of carbon dioxide at the pharynx of 3.5 to 6 per cent, at the lips 2.5 to 4 per cent, and in the rebreathing bag 0 to .02 per cent during anesthesia using the technique.

With a completely closed system for anesthesia, the water vapor contained in each expiration is retained in the enlarged respiratory tract. The atmosphere will soon be completely saturated with moisture. The cooling effects of the air surrounding the breathing bag during a long narcosis will result in some condensation in the bag. Although the optimum humidity of respired anesthetic mixtures is not scientifically determined, one needs only recall the fact that dehydration has long been an accompaniment to protracted inhalation anesthesia and to note its absence with the closed system to conclude the advantage of the latter. Moreover, with open techniques the patient expands no small amount of energy in moistening anesthetic vapors. This has been reduced to calories by Connell[22] who estimates a saving of some 150 to 200 small calories per minute when breathing moistened anesthetic vapors. The high humidity has a practical effect in reducing the fire and explosion hazard of anesthetic agents. Explosions are initiated from outside the anesthetic apparatus and start at an outlet of the explosive mixture. The closed system has no outlet. Static sparks may be produced only in an atmosphere of less than 54 per cent humidity. With the closed system the atmosphere is 100 per cent humid.

With the entirely closed system the temperature of the atmosphere inspired is increased by the heat generated during the chemical reaction between the alkali and carbon dioxide. With good grades of soda lime this temperature has been found not to exceed 40°C. at the point of maximum reaction,[21] an entirely safe temperature. It does not follow that the average

inspiration of less than 500 c.c. of gases warmed to less than 40°c. will produce an atmosphere at the alveoli with such a temperature. It is unlikely that dilution of the four liters of gases in the lungs by one-eighth of its volume, in an atmosphere of slightly higher temperature, will be an imposing factor in disturbing physiological heat regulation. Breathing a cold dry atmosphere is known to result in irritation of respiratory membranes, to stimulate respirations, and tend to decrease body temperatures and increase perspiration. Although the thermoregulating center may be directly effected by the anesthetic action on the hypothalmic area, it is quite possible that breathing a warm atmosphere may eliminate some sensory impulses to that area. It is a consistent clinical observation that while using the carbon dioxide absorption method, there is a tendency toward a rise in body temperature and the regulation of body heat by perspiration is not a common occurrence. Moreover, the patient's energy ordinarily needed to warm anesthetic vapors is conserved and a satisfactory heating device to assist the volatilization of ether without danger of oxidation or increasing the fire hazard is provided.

Advantages in addition to the physiological control of carbon dioxide and oxygen as well as temperature and humidity, have often been cited for the complete rebreathing of anesthetic mixtures. The absence of increased muscular activity incident to hyperactive respirations has added convenience to surgical manipulations within the abdomen and decreased the possibility of activating latent lung pathology. The fire and explosion hazards are greatly minimized. The surgical team may work in an atmosphere free from obnoxious or toxic anesthetic gases. An enormous economy is effected. The anesthetist is provided with a convenient technique that is not laborious and readily permits frequent and essential observations of the patient, his blood pressure, pulse and muscular reactions, which are so essential in proper management of the case.

To use the technique successfully, one needs have a clear appreciation of the physiological symptoms accompanying oxygen deprivation, carbon dioxide excess or depletion, and overdose of the agent in use. He must be aware of asphyxia with or without retention of carbon dioxide, with or without increased respiratory movements and, particularly, with or without cyanosis. Too often the anesthetist may become indifferent to the basic principles of the technique. The absorption unit may be omitted from the system until excessive carbon dioxide permits rapid etherization and surgical anesthesia is more quickly obtained or extremely high concentrations of carbon dioxide may be unwisely used to simplify tracheal intubation. These savings of the very few minutes time to the anesthetist and surgeon are not rarely won at the patient's expense. The contribution of carbon dioxide absorption, from anesthetic mixtures and complete rebreathing, represents a real advance in the efforts to administer inhalation anesthesia without physiological disturbances but it offers no substitute for lack of knowledge, experience and skill of the person using it.

SUMMARY

Like most revolutionary innovations and discoveries in the art and practice of medicine, the absorption of carbon dioxide from anesthetic mixtures was not first used by accident nor was it the creation of one individual. It resulted from the intelligent application of accumulated knowledge of anesthetics and their administration. D. E. Jackson applied the principles of complete rebreathing of anesthetic mixtures to laboratory experiments; Ralph M. Waters established the method in clinical anesthesia.

The absorption of carbon dioxide from anesthetic mixtures introduces desirable improvements in inhalation anesthesia. Accurate, convenient and safe appliances have been constructed. Anesthetic mixtures may be completely rebreathed. The

respired atmosphere is warmed and saturated with water vapor. The physiological control of carbon dioxide and oxygen tensions, essential during inhalation narcosis, may be accomplished by the anesthetist. The fire and explosion hazard is minimized. Obnoxious and toxic anesthetic gases and vapors are removed from the atmosphere breathed by the surgical team. A definite economy is effected. A convenient technique that improves surgical conditions is available. The technique to be employed satisfactorily requires clinical judgment as well as technical ability.

REFERENCES

1. Servetus, Michael. "Christanism Restitutio," 1553.
2. Harvey, Wm. In: "Bibliothea Osleriani." Clarendon Press, 1929.
3. Hooke, Robt. *Phila. Trans. Roy. Soc.*, London, 1: 194, 1809.
4. Lavoisier, Antonio. In: Hist. L'Acad. Roy. Sci., Paris, 1775.
5. Mayon, John. Tractatus quinque Medico-physici. Oxford, 1674.
6. Spallanzani, L. Memoirs on Respiration. London, 1804.
7. Black, J. In: Thomason "Carbon Dioxide Absorption." *Anesth. and Analg.*, 6: 181 (Aug.) 1927.
8. Brindley, G. and Foregger, R. "Experiments with fused sodium peroxide." *Trans. Amer. Electrochemical Soc.*, May, 1906.
9. Brown, E. W. Value of high oxygen. *U.S. Naval u. Bull.*, 28: 523 (July) 1930.
10. Jackson, Dennis. *Jour. Lab. and Clin. Med.*, 1: 1–12 (Oct.) 1915.
11. Waters, R. M. Carbon dioxide absorption. *Ann. Surg.*, 103: 38 (Jan.) 1936.
12. Haldane. Smithsonian Contribution to Knowledge No. 989. Washington.
13. Lee, F. S. Ventilation. *Report N. Y. State Comm.*, 1923.
14. Gatch, W. D. Use of rebreathing. *J. A. M. A.*, 57: 1593 (Nov.) 1911.
15. Boothby, W. and Cotton, F. In: Gwathmey, Anesthesia, 1914.
16. Wilson, Lamb and Cheney. Chemical Warfare, vol. IV, No. 3, 4, 5, Edgewood, Md., U. S. Govt., 1920.
17. Benedict and Tower. *Jour. Am. Chem. Soc.*, 21: 396, 1899.
18. Haggard, H. W. The absorption of anesthetics. *Anesth. and Analg.*, 5: 16 (Feb.) 1926.
19. Hill and Flack. Effects of oxygen and carbon dioxide. *Jour. Physiol.* (June 30) 1908.
20. Haldane, J. S. Respiration. Yale Univ. Press, 1927.
21. Waters, R. M. Carbon dioxide absorption. *California and West. Med.*, 35: 342 (Nov.) 1931.
22. Connell, K. In: Woodbridge, Carbon Dioxide Absorption. *Anesth. and Analg.*, 12: 161 (July) 1933.

INHALATION ANALGESICS IN OBSTETRICS

ANSEL M. CAINE, M.D.

Anesthetist, Touro Infirmary and Southern Baptist Hospital

NEW ORLEANS, LA.

THERE are at the disposal of the anesthetist who wishes to alleviate the pains of the parturient woman, several inhalation agents capable, when properly administered, of relieving the pains, either completely or to a large extent, without appreciably slowing the progress of labor.

By the term analgesia, in this paper, we mean that stage of anesthesia just before consciousness is lost but in which the pains associated with uterine contractions are dulled or abrogated entirely. Hearing, while present, is not always perfect. Often there is a blissful feeling with a numbness over the entire body. The patient will sometimes say that she feels funny. Some will lie perfectly quiet between pains; others will toss about. Often there will be an expression of gratitude. This stage, if it may be called a stage of anesthesia, is quite narrow and requires experience and skill to secure and to maintain with fair uniformity. To be satisfactory, suffering should be relieved and the progress of labor not appreciably slowed.

Inhalation anesthetic agents, when administered for this purpose, are called analgesics. They are of two classes, (1) those normally liquid and not bulky, and (2) those normally gaseous, coming to us in more or less bulky containers. Of the former, there are two in common use, ether and chloroform; of the latter there are three that are well known, and two in common use. The ones in common use as analgesics are nitrous oxide and ethylene. The third, cyclopropane, has not as yet been used to any great extent in obstetrics. Vinethene is left off the list because Bourne's experience led him to say that it was almost impossible for him to secure analgesia with it.

Choosing the analgesic for any given case is both positive and negative. The choice is influenced by available agents at the time; by knowledge of how to use them and what to expect from them; by climatic conditions; by proper apparatus at hand; by the condition of the patient; by the opinion of the obstetrician; and by the presence of a skilled anesthetist.

The lone practitioner will certainly not be expected to have at hand in his obstetrical kit an assortment of gaseous agents, an expensive gas machine, and a professional anesthetist. He will probably be his own anesthetist, his own nurse, his own obstetrician, and his own supervisor. His anesthetic equipment must be of the simplest, and his agents at hand will usually be ether and chloroform. His equipment will probably be a mask and a drop bottle or drop can. The question is how can he get the most effective and safest action from his equipment.

Here is a suggestion for the choice of his mask: have one with a chimney, which can be bought or it can be made from his present mask by fastening upright wires about four or five inches long to the ring that holds the gauze in place. These should be firmly soldered in place, and should be of the type of wire that is tough and will not bend easily, and that will not rust. Another ring of wire, similar in size and shape to the one that holds the gauze to the mask, connects the uprights at the top. A towel can be pinned around these uprights, thus forming a chimney, or a piece of old inner tube can be used for the same purpose. Gauze packed lightly in this chimney will hold the desired amount of chloroform or ether to be used for that particular pain. This prevents the possible burning of the patient's eyes or face with

the agent, and promotes quick evaporation and faster action. Since in this way most of the anesthetic will be used by the patient, there being very little waste, care is necessary not to put too much on the gauze. If using chloroform, it is much better to drop it on the mask than to pour it on. The agent is not safe and the boiling point high. All of it may not be evaporated at each use, so a considerable amount might accumulate on the gauze and more taken by the patient than desired or intended.

When it becomes necessary to go from analgesia to anesthesia, and some relative or similar emergency pick-up has to handle the mask and anesthetic agent while the obstetrician's attention is necessarily diverted, if chloroform has been used for analgesia, it is far safer for a switch to be made to ether, as the margin of safety is much greater.

This arrangement is not ideal, but this obstetrician (and he is numerous) is not working under ideal surroundings.

When used as interrupted analgesics both ether and chloroform have a hangover which is sufficient to relieve considerably the continuous backache between pains, when they are close together.

With the mask described, 2 or 3 c.c. of ether will suffice to give a fair analgesia, but it must be given at the first indication of approaching uterine contraction as its action is not as fast as that of the gases.

Chloroform always does damage to the liver and kidneys; it is a matter of degree and not of kind. But probably normal patients who receive it for analgesia only, rarely suffer irreparable damage. Ether is safer for these patients, and, while not quite as efficient as an algesic, should, of the two, be the agent of choice.

Where necessary apparatus, agents, and help are available some one of the three gases mentioned should be the choice.

In order of use over the country for this purpose, probably they would be nitrous oxide, ethylene and cyclopropane, while in their order of efficiency as analgesics the arrangement will probably be reversed. However, there are angles to be considered in connection with each gas that might influence the decision of which to use.

In some localities the matter of whether the gas is explosive or not is of great importance. This is specially true where the normal humidity is low, or where it is low because of low temperature. Static abounds where it is cold and dry, and a static spark is very common. Under proper conditions this spark is sufficient to ignite the gas and cause loss of life or great damage. So when this has not been thoroughly guarded against either by raising the humidity, which is the most efficient and cheapest way to cut down this hazard and least subject to error in technique; or by thorough grounding, which is more or less complicated and more subject to error in technique, it is wise to choose the non-explosive gas, nitrous oxide.

The apparatus used will influence the choice. If an interrupted flow, automatic cut-off machine is used, like the old McKesson, it is not practical to choose cyclopropane; the expense would prohibit it. Either nitrous oxide or ethylene would be the choice because they are at present much cheaper. Yet where interrupted analgesia is desired with nitrous oxide or ethylene, such a machine is preferable, in our opinion. When the desired and required mixture of oxygen and nitrous oxide, or etheylene, is found for that patient, it is easier to secure such uniform percentage with the interrupted flow machine than with the continuous flow type where the mixture of gases is trapped in a bag, subject to marked dilution with the air in the lungs when inhalation is begun at each pain. Even with cyclopropane, where the percentage required to give analgesia is ordinarily low, the percentage in the bag must be kept high to be satisfactory, and fair uniformity of percentage from pain to pain by this technique is not easy to maintain. This is true even with a hand cut-off in the head of the mask, like in the Heidbrink or Foregger machines. With this type

of machine good interrupted analgesia can be secured with C_3H_6 however, and that was the technique followed by Wesley Bourne and Ralph Knight in their first reports on the use of cyclopropane in obstetrics.

The physical condition of the patient will influence the choice of the agent. It is not wise to suboxygenate a diabetic. Ethylene or cyclopropane would be the choice in such cases, preferably the latter. Toxic cases do better with a high percentage of oxygen also.

It also influences the technique. Overexercising a tubercular lung, active or dormant, would be bad and should never be practiced.

Great care both in technique of administration and coaching of the patient should be exercised in heart cases, so as to reduce to a minimum the tax associated with bearing down.

Inhalation analgesia may be begun after three fingers dilatation when pains are good, but when begun this early it is often quite protracted. From an economic standpoint it is better to wait to near complete dilatation, depending on barbiturates, paraldehyde, and scopolamine, in combination with morphine, pantopon, dialudid, or heroin, (when it can be had), to secure analgesia in the first stage. However, if deemed wise by the obstetrician and anesthetist in a certain case to start gas this early, no harm will result to mother or child. Analgesia is started earlier in multiparas than in primiparas.

Inhalation analgesia may be of two types, interrupted and continuous.

As stated, interrupted analgesia is best secured with nitrous oxide and ethylene with the interrupted automatic cut-off type of machine. The reason for this is that the percentage of these gases for quick analgesia must be fairly high in the lungs at the time the breath is held when the patient bears down after full dilatation. The technique is simple. Explain carefully to the patient what to do and how to do it. If she is not under the influence of drugs such as are mentioned, good cooperation can often be secured and an analgesia rendered much easier. With ethylene the dial on the mixing chamber is set at 75 ethylene, 25 oxygen. When a pain approaches, the mask is placed snugly on the face and the patient is instructed to breathe deeply, then to expel it all, again to breathe deeply, again to expel it all, then she is told to hold the next breath and bear down (if the anesthetist's other hand tells him the contraction is on). When she forces as long as she can (or will), she inhales again and is told to hold that breath and bear down as before. This is repeated until the contraction begins to fade. When the pains are long, extending through more than two long periods of breath holding and bearing down, it might be found necessary to raise the percentage of oxygen to prevent anesthesia. If she has done well, she is encouraged, if not, she is further instructed, but not condemned. The deep inspiration and forced expiration are essential to success by this method for the reason stated, and by deep inspiration and forced expiration, without rebreathing, the mixture of gas and oxygen in the lungs at the end of the third breath approaches that in the mixing chamber of the machine, and, when the breath is held, sufficient gas is taken into the blood and sent over the short route to the brain to produce analgesia. The above mixture may not be exactly right, but this will be determined by the anesthetist after the first few pains. When cooperation is good and the mixture right, the patient will usually let you know. If the mixture is not right or there are choppy, short inspirations and expirations the analgesia will not be good.

The technique with nitrous oxide is the same, except that less oxygen is used in the mixture.

You will note that the use of gas by this technique is rather extravagant. But with these two gases dilution with air is not concomitant with best results.

The technique for *interrupted analgesia* with cyclopropane has been partially de-

scribed. A machine with soda lime attachment for CO_2 absorption is essential. The absorber should be at a distance, as in the "circle absorber" type, so as to allow the patient freedom of motion of the head. There must be a hand cut-off in the head of the mask to prevent the loss of gas when the mask is removed.

The bag is about half filled with a 25 per cent to 40 per cent mixture of C_3H_6 in oxygen, the hose being attached, and the cut-off in the head of the mask at off. At the approach of the pain the mask is applied snugly to the face with the valve in the head of the mask closed. At the end of the first expiration which should be forced, if cooperation can be secured, the valve is quickly turned on and the patient breathes deeply, holding the second, third, or fourth breath as found best, and as described in interrupted analgesia. When the pain begins to subside the mask is removed, after the valve in the mask is turned off *at the end of expiration*. With minor modifications this is the technique. It will readily be seen that the mixture in the bag and hose is different now from what it was at the beginning of the pain, having been diluted with the air residual in the patient's lungs when the mask was applied. To maintain the percentage in the bag to the desired level, a little cyclopropane must be added, if not after each pain, after every second or third.

By *continuous analgesia* we mean that the mask is applied snugly and strapped on comfortably, and the patient allowed to breathe an analgesic mixture of the gas and oxygen continuously, rebreathing through soda lime, and adding a continuous flow of oxygen sufficient to meet her metabolic requirements just as in anesthesia.

For this type of analgesia to be satisfactory, a comfortable fitting mask and retaining strap are essential. The hose leading to the soda lime absorber must be long enough to allow the patient to move her head without a pull sufficient to annoy her or to tilt the mask on the face and cause a leak. The hose on the usual circle absorber is long enough for this. Then the hose must be light and not easily kinked. The soda lime should be active so as to prevent all feeling of suffocation on the part of the patient. *This is essential.* The absorber must be far enough away to allow the rebreathed gas to cool sufficiently to be comfortably inspired by the patient.

Any one of the agents may be used.

Sword described the technique with nitrous oxide and was much pleased with the results. Griffith stated that he had tried it and liked it also. Others, of course, have used it.

The technique is the same with each gas, but the percentage of oxygen varies. Ethylene admits a much higher percentage of oxygen than nitrous oxide, and is a better anesthetic when anesthesia is needed. Cyclopropane admits a still higher percentage of oxygen, gives excellent analgesia without slowing the pains, and can be deepened to excellent anesthesia for episiotomies, forceps delivery, etc., within a very short time. It is very flexible, but the percentage required to produce analgesia may differ but little from that producing complete loss of consciousness. We commence with the bag about half full of oxygen to which about 500 c.c. of cyclopropane has been added. The mask is applied between pains and strapped on so that the patient can tell if it is comfortable. She is told that it will not be removed and that her contractions will continue but that there will be no pain. The valve in the head of the mask is now turned on at the end of expiration. When pains come on she is told to bear down, if such is desired. It may be necessary to add some cyclopropane, which will be determined after the first few contractions, although the opposite may be true. Oxygen is added to lower the percentage if necessary. As stated, a continuous flow of oxygen sufficient to meet the metabolic requirements, is maintained.

The advantage of continuous analgesia is that after securing the proper analgesic dose, there is uniform maintenance; the

backache between pains is done away with; the danger of explosion is at a minimum; one type of machine can be used for all the gases; actual cost of material is reduced to a minimum.

When the head has reached the point on the perineum where it does not recede between pains, we deepen the stage to light anesthesia, if all is well. If labor is too rapid, we deepen the anesthesia and slow the labor to lower the incidence of lacerations. The technique here varies with the varied opinions of the obstetricians.

At this stage we usually accumulate some carbon dioxide in the mixture being breathed by the patient, because of its influence on the uterine contractions after the baby is born. But in breech cases we do not accumulate CO_2 until after the delivery. This also holds good for versions of course.

Since the excellence of the anesthesia that can be obtained with C_3H_6 has been mentioned, a word should be added concerning anesthesia for versions. It will be found safer for the baby and the mother and easier for the obstetrician if deep anesthesia is secured before attempt at version by the operator. By deep anesthesia I mean *profound*, where the uterus is relaxed. To secure this, ether or chloroform is required, and oxygen should be administered with them in excess. In other words, if these agents are added to the gas used, as anesthesia deepens, excess of O_2 should be added. The added danger of such profound anesthesia is more than compensated by the reduced shock of the intra-uterine manipulation, and the lowered infant mortality.

SUMMARY

1. The pains associated with the first stage of labor are probably more practically controlled in other ways than by the use of inhalation agents.

2. In the second stage inhalation analgesia works more satisfactorily, and is better controlled.

3. While any of the anesthetic agents in general use may produce analgesia, the gases, nitrous oxide, ethylene and cyclopropane, are safer and more flexible than ether or chloroform.

4. Ethylene and cyclopropane will produce better analgesia than nitrous oxide.

5. With skilled anesthetists available, continuous analgesia is very practical, and the consumption of the anesthetic agent is reduced to a minimum.

6. The functions of the anesthetist in a labor case are many. He must keep up the morale of the patient; produce real analgesia and not a mere camouflage; cause her to work when work is indicated, and to slow down when that is deemed best; be ready and able to produce any stage of anesthesia necessary in the safest known way. Last, but not least, keep up with all that is known about infant resuscitation and be prepared to execute it.

ANESTHESIA IN CHILDREN

C. H. Robson, M.D., C.M.

Anesthetist-in-Chief to the Hospital for Sick Children, and the Hospital for Consumptives; Clinical Demonstrator in Anesthesia, University of Toronto

TORONTO, ONTARIO

THE administration of agents for the establishment of anesthesia in infants and in children to the age of fourteen, presents some aspects which differ from the methods employed in adults, and in this article are presented the results of our experience in the Hospital for Sick Children.

In the case of these little ones, we are dealing with organisms which tolerate, and, indeed, require relatively larger doses of anesthetic agents, sedatives and hypnotics than do adults. This is to be attributed to their higher metabolic rate, which approaches that of the hyperthyroidic adult. This statement does not imply that general anesthetics may be administered with a lavish hand without danger. On the contrary, the margin between safety and danger may be narrow and it is here that experience in caring for children undergoing and during anesthesia plays such an important part in their safety and comfort.

The word "comfort" has a world of meaning for these little ones. How often have we had children brought to the anesthetic room by fond parents who have deceived them as to what is about to take place. It is no wonder that, expecting "the doctor to look at the throat," they should resist when held down on the table, a mask placed over the face and a strange smelling substance dropped on it. Some of these disagreeable experiences are far reaching in their effects; often associated with fear of falling asleep or with terrors at night. A much easier course is experienced by the patient and by the anesthetist when the various steps leading up to unconsciousness are explained to an amenable child. On the other hand, I do not suggest that a child, due for tonsillectomy, should be told a week in advance of the contemplated operation, for it is almost beyond belief what terrors are sometimes portrayed by playmates. Later, we shall deal with means of establishing mental comfort.

Preoperative preparation differs from that in the adult in one very important aspect. Children are more liable to the postoperative condition of the so-called acidosis. Depletion of the glycogen reserve predisposes; therefore ether and especially chloroform should not be administered to one in such a condition. Some years ago we had 2 fatal cases in children of about twelve years of age. They were in good physical condition prior to being anesthetized for simple operations of an elective nature. Excessive vomiting with acetonemia began a few hours afterwards and despite all treatment, terminated disastrously.

Immediately we established routine measures to insure a carbohydrate reserve and a proper alkaline balance. Various types of gruels were given prior to operation but it was found that digestion was delayed due, chiefly, to psychic influences. Our routine now is plain sugar or the juice of one orange in a glassful of water, sweetened with a tablespoonful of corn syrup, given at least two hours before anesthesia. In acute abdominal cases where vomiting and loss of fluids have been excessive, a preoperative intravenous of glucose 5 per cent in saline is given. The volume is estimated at 15 c.c. per pound of body weight. For operations of an elective nature in infants the regular feedings are continued up to the time of operation which is fixed to take place at the time of the next regular feeding. I should like to stress the importance of this, for the administration of an

anesthetic such as ethyl chloride, ether or chloroform for even a short period, may bring disaster to an improperly prepared child.

At this point it is opportune to deal with the cases which have had too much food taken too recently. Deaths are recorded from asphyxia by inspired food particles, following operation. When food has been taken shortly before an accident or an emergency operation, the anesthetist is confronted with the problem of emptying the stomach. The effects of injury or of the sudden onset of illness on the progress of digestion should not be overlooked. Normally the stomach should be empty after three or four hours, but experience has taught us to expect the vomiting of large quantities of food as long as six or eight hours after ingestion. Mental influences such as fear and anxiety also exert a retarding action on digestion. Obviously the dangerous large particles of food will not pass up a stomach tube. Apomorphine is a depressant and should be avoided. Violent vomiting efforts are, in the conscious state, painful to the site of injury in many cases. The method we employ is to place the patient on one side on the table, induce anesthesia with ethyl chloride followed by ether up to the point where the swallowing reflex is abolished. The mouth is now opened with a gag and after a few seconds the pharyngeal reflex returns to the point where stimulation with a tongue depressor induces vomiting, the stomach emptying itself without distressing the semiconscious patient. In the case of the infant to be operated for pyloric stenosis, the fluid content of the stomach is drained off through a small stomach tube in the conscious state. This step should never be neglected for the manipulation of the stomach containing fluid will cause the contents to pass up the esophagus and obstruct the airway.

PRELIMINARY MEDICATION

Mental comfort in these little patients may be established, induction of anesthesia made smoother and a reduction in the amount of the agent used, by the proper administration of sedatives and hypnotics. Most publications state that "Morphia is badly tolerated by children and by the aged." The statement is true in regard to the latter age, but is certainly not true in regard to children. Not only does our clinical experience teach us that it is not true but we find that children require relatively larger doses than do adults, to obtain the necessary therapeutic effect.

We have given an eight year old boy ¼ gr. of morphine hypodermically in doses of ⅛ gr. at half hourly intervals. This dose is cited only as an illustration of the tolerance of children.

A recent addition to the premedicants are the barbiturates and the one employed for administration by mouth is nembutal. Some children find it difficult to swallow the capsule, in which case the powder is dissolved in a teaspoonful of water. When a gas anesthetic is to be administered the routine dosage is, according to age, as follows:

Years	Nembutal	Morphine (Hypo)
4	½ gr.	1/12 gr.
6	¾ gr.	1/10 gr.
8	1 gr.	⅛ gr.
10	1 gr.	⅙ gr.
12–14	1½ gr.	⅙–¼ gr.

The nembutal is given one hour previous to anesthesia and followed in fifteen minutes by the hypodermic injection of morphine. When the anesthetic is to be ether the dosage is dropped back to the next younger bracket. The dosage for ether anesthesia would be tabulated thus:

Years	Nembutal	Morphine (Hypo)
4	¼ gr.	1/16 gr.
6	½ gr.	1/12 gr.
8	¾ gr.	1/10 gr.
10	1 gr.	⅛ gr.
12–14	1 gr.	⅙ gr.

In children under four years of age codeine is used hypodermically. A two year old child is given ¼ gr. and a one year old ⅛ gr. Under one year no sedatives are used.

Paraldehyde was tried in a series of cases but was discontinued because of its disagreeable taste and its uncertain effect, in favor of the nembutal-morphine sequence.

No atropine is used as it is felt that it serves no useful purpose and has many disadvantages; the dryness of the mouth and throat is very distressing; the loss of normal moisture in the alveolar walls prevents a free interchange of gases; it definitely retards the ciliary activity of the respiratory mucosa and many of the rises in body temperature (as high as 102°) in children are due solely to the effect of atropine. So, if a child comes to the operating floor with a temperature higher than our uppermost limit of 99.2°, we should be at a loss as to the cause. Is it an atropine effect or the onset of one of the infectious diseases of childhood?

Obviously, the chief reason for the employment of atropine is to diminish the output of mucus and saliva. In a later paragraph we shall state what steps we use to prevent the obstruction of the airway by mucus and saliva.

No morphine is given to children for tonsillectomy or for any operation on the nose or sinuses since we wish the reflexes to return to normal as quickly as possible to guard the respiratory tract against the entrance of blood.

ROUTINE ANESTHETIC

In this hospital the agent mostly used is ether by the drop method (open). In almost all cases it is preceded by ethyl chloride. I am fully aware that I am opening up a very controversial subject but I am also fully satisfied that ethyl chloride is a safe drug when properly employed. It has no equal as a preliminary to ether. A detailed description of the method may be permitted here.

The child is placed on its side and a Yankauer mask covered with ten layers of loose meshed gauze is put over the face. The stockinette covered mask, so frequently used, becomes too impervious to the free passage of air when moistened and is a contributing factor to so many bad inductions. The patient is instructed to blow out through the lips, making a sound that is audible to the anesthetist. This is a psychological trick but a very effective one. Moreover it is a natural impulse to blow away a strange smell. Ethyl chloride is dropped on the mask at the rate of one drop a second for half a minute, then increased to two drops a second until the child is unconscious and the movements felt below the floor of the mouth have ceased; or to the point where ether vapor in high concentration will be tolerated. Ether is now dropped on freely and usually anesthesia by this drug is established before the effect of the ethyl chloride passes off. Should, however, the effect of the ethyl chloride lighten before anesthesia by ether is established, as shown by coughing, laryngeal stridor, etc., we do not hesitate to drop on a few more minims of ethyl chloride and so by overlapping the effects of the two drugs obtain surgical anesthesia. It is the exception for us to have any crying or struggling with this sequence, even in children who have had no preliminary medication.

I cannot too strongly stress the drop method of using ethyl chloride. Beyond a doubt, the rapid onset of signs of overdose, as shown by pallor, great depression of the circulatory system and respiratory arrest, cannot always be avoided if the drug is sprayed on the mask. The mechanics of the two methods may be stated thus; when dropped on the mask the liquid passes into a vapor on the outer layers of the gauze and is inhaled with a plentiful supply of air. When sprayed on the mask the stream is driven through the gauze and becomes a gas in the limited confines within, with the result that the patient inhales a very high concentration of ethyl

chloride which may quickly lead to overdosage.

No towel or other covering is placed around the mask for it is felt that, with a free airway and full ventilation, no greater concentration than that given off from the gauze is necessary.

POSTURE

In the last paragraph the importance of a free airway was noted. This leads us to a reference to atropine. When this drug is not used to suppress the outflow of saliva and mucus, some means must be employed to prevent their entrance into the respiratory tract with subsequent interference with free ventilation. We do this by making use of gravity. The child is placed on one side with the shoulders and pelvis on a plane perpendicular to the table. A very small pillow is placed under the head. The lower cheek now forms a pocket in which the fluid secretions collect, and from which they are drained by depressing the angle of the mouth. This lateral position has additional advantages:

1. It is a normal position for the child to assume for sleep.
2. The tongue falls forward and there is no need for the use of a tongue forcep.
3. Any excess ether drops from the lower edge of the mask and so any danger of it reaching the eyes is avoided.

When surgical anesthesia is established the patient is placed in any suitable position for operation but the head is kept turned to the side as far as is possible without pressing the larynx against the hypopharyngeal wall by the transverse tension on the neck muscles.

Several other points in regard to posture arise here. Many a patient is figuratively and literally "looking toward Heaven" when he is lying in an anesthetic state with his face directed upward.

Having taken every precaution to obtain and maintain a free airway during anesthesia, many anesthetists miss the importance of placing the patient on his side immediately he is transferred to the stretcher to be taken to his room. Moreover he should be put on his side in bed and turned from side to side at intervals of not more than thirty minutes, as long as he is unconscious.

Many surgeons wonder why their patients complain bitterly of pain in the lumbar region following operations of some length. In fact they may not complain of any pain at the site of the wound, so overwhelming is the distress in the back. This condition is met in adults rather than in children. The problem is one of mechanics. When the musculature is relaxed under anesthesia, the weight of the thighs causes the pelvis to pivot on the ischial tuberosities producing a marked lordosis of the lumbar vertebras. The prolonged abnormal pressure on the articular surfaces produces pain. The placing of two large pillows under the patient's knees, while on the operating table, prevents the forward curvature and thus spares the patient this unnecessary pain.

OTHER AGENTS AND METHODS

While ether is the chief anesthetic employed and usually by the open method, it is also used in endotracheal insufflation during operations on the eye, sinuses, intranasal work, brain operations and other procedures on the head and neck. Lobectomies are also done under this method.

Chloroform is considered to be too dangerous a drug and we do not use more than two ounces a year and that chiefly as a rapid inductive agent preceding ether, in cases suffering from bronchiectasis, for the passage of a bronchoscope for the removal of secretions by suction.

Nitrous oxide is a very poor anesthetic agent for children and its chief use now is in the *x*-ray room. It has been replaced by cyclopropane which is giving most excellent results. In this drug we have an agent which gives full relaxation in abdominal work with a contraction of the bowel

resembling that obtained under spinal analgesia. Induction is pleasant and rapid. No element of cyanosis is present. Recovery is speedy and postoperative vomiting very little in excess of that following the use of nitrous oxide.

We have had no cases of laryngeal spasm which occasionally happens in adults. There have occurred, however, a percentage of cases of sufficient number to warrant reporting. These are cases where the laryngeal spasm comes on early in the recovery period. Shortly after the removal of the facepiece, the child vomits and there is a spasmodic closing of the larynx. Cyanosis is present, the pupils dilate, the circulation is markedly depressed and breathing efforts cease. This is a result of the effect of the cyclopropane, still in the blood stream, acting on the centres in the presence of anoxemia.

I have found it necessary on several occasions to pass a catheter quickly into the trachea and, by blowing through it inflate the chest, two or three inflations being sufficient to start respiration. Recovery is rapid and uneventful. Our practice now is to insert a mouth gag immediately on removing the face mask, turn the patient on one side and suction off any vomited fluid. No patient should be sent to the ward directly upon removal from the table. A few minutes spent in tending the early vomiting spell which is nearly always present, may avoid disaster.

We are particularly impressed with cyclopropane in operations for spinal bone grafting for tuberculosis and for the more extensive grafting for the correction of scoliosis. These procedures are of long duration and productive of a great deal of surgical shock. Up to a year ago, we used ether by endotracheal insufflation, now we use cyclopropane, also endotracheally, through a soft rubber catheter which fits the glottis gas-tightly. These cases have shown a very marked lessening in the amount of shock, a greatly improved condition on leaving the table and less postoperative reaction.

AVERTIN

Due to the fact that it requires long postoperative observation on the part of the recovery nurses, it does not lend itself well, as a routine agent, to large institutional work. We use it only where it is especially indicated. Children require relatively larger doses than do adults. Our usual dose is 90 to 100 mgms. per kilo as a basal. We do not exceed 120 mgms. in any case.

SPINAL ANALGESIA IN CHILDREN

There is a definite place for this means of abolishing pain in children, but it is limited. We feel justified in using spinal only when some one or other of the general anesthetics is not suitable. We believe that there is less risk in giving a spinal to a child than there is in giving it to an adult; nevertheless, we prefer some form of general anesthesia.

In the case of the child there is distinctly less reaction to the effects of the absorption of novocaine. Owing to its more elastic and reactive circulatory systems, there is not seen the same fall in blood pressure as is noted in the adult. We have used this method in all ages of infants and children; from the few-hours-old infant upward, for all sorts of operations within the abdomen and operations on the skeleton. A series of cases of lobectomy was done under spinal but this class of case is now given ether by the endotracheal method through a catheter sufficiently large to permit the passage of a fine suction tube for the removal of secretions.

The use of spinal is now confined to cases:

1. Where considerable surgical shock is anticipated, as in reconstruction operations on the hip joint;
2. Where there is to be extensive intra-abdominal manipulation;
3. Where the patient must be spared the general intoxication and the depressive

after-effects of a general anesthetic agent. At this point I should like to stress two "don'ts":

(a) Do not give a spinal to the case showing abdominal symptoms of a possible appendicitis, where an early pneumonia is also suspected; and

(b) Do not give a spinal to the case showing abdominal symptoms and an acute infection of the throat is also present. Both these cases may have a bacteriemia and the injury caused by the needle puncture may focus the infection in the spinal canal. Use cyclopropane.

The technique is exactly that commonly used in adults. For infants we made our own needles by cutting off the proximal one inch of a number 22 needle, bevelling the end and sharpening it on a razor hone. Similar needles of 1¼ and 1½ inches were made for larger children. The site of puncture should be in the space between the third and fourth lumbar spines, for it must be remembered that in children the cord does not break up into the cauda equina at the level of the first lumbar, as in the adult, but extends much lower and may be damaged by the needle if a puncture is attempted higher up. The rate of injection is slower than in adults, where 1 c.c. is introduced per second. The timing usually used is three seconds per c.c.

Dosage. For infants for such operations as that for pyloric stenosis 20 mgms. are dissolved in 1 c.c. of spinal fluid. For older children our working rule is to give 10 mgms. for each year of age for an analgesia reaching to the costal margin. Thus an eight year old child would be given 80 mgms. dissolved in 3 c.c. of spinal fluid. Ephedrine is used only when the spinal effect is to extend above the umbilicus.

The preliminary sedative is that used for ether anesthesia.

ETIOLOGY OF MUSCULAR SPASMS DURING GENERAL ANESTHESIA

EDWARD C. ROSENOW, M.D. AND RALPH M. TOVELL, M.D.*

Division of Experimental Bacteriology, The Mayo Foundation

Section on Anesthesia, The Mayo Clinic

ROCHESTER, MINNESOTA

IN 1880, Humphrey first noted muscular activity of a trembling yet rhythmic type occurring during the administration of ether by inhalation. During the years of the World War this manifestation was reported by several observers.[1,3,6,9,37,78,79] The condition is known as "ether clonus" or "ether rigor"; it usually occurs in the course of induction of anesthesia; the tremor frequently is limited to the lower limbs and ceases as anesthesia deepens. In 1916, Mytinger reported his experiences in anesthetizing 100 patients suffering from idiopathic epilepsy. Epileptiform convulsions occurred frequently in the stage of induction of anesthesia. In 1922, Patch reported 2 cases in which epileptiform convulsions occurred in the course of anesthesia, in only one of which was epilepsy known to be a factor. Both patients recovered. It is in this group of individuals who do not have epilepsy that we are particularly interested at this time. In 1927 Wilson, anesthetist at Manchester Royal Infirmary, reported 4 cases in which "ether" convulsions were fatal in 1926. Pinson,[52] on the same date, reported 15 cases in which convulsions occurred in the course of general anesthesia, in nine years experience, including 11,000 administrations. Following the appearance of these articles, 12 more cases appeared in the literature in 1927,[13,21,23,24,28,34,38,45,48,53,70,84] 9 in 1928,[10,18,26,29,46,47,68,77,81] one in 1929,[54] 8 in 1930,[22,25,35,55,58,66,71,74] 15 in 1931,[4,5,7,11,14,15,27,30,31,32,43,44,56,69,82] 5 in 1932,[17,19,33,36,75] 4 in 1933,[40,67,80,87] 6 in 1934,[8,12,20,57,72,76] 9 in 1935,[2,16,41,50,65,73,83,85,88] and one in 1936.[86]

Although there is wide diversity of opinion regarding the cause of this complication there is uniformity in the description of the syndrome. The patients are frequently children or young adults. Many are suffering from acute infections associated with pyrexia. Ether is the agent that has been most frequently associated with the syndrome, although frequently it has been administered as a vapor, with oxygen or with nitrous oxide and oxygen. Bull reported one case in which chloroform was used. Respiration is usually rapid and is labored to some extent but frequently the first untoward sign noted is twitching of the muscles of the face, occurring during the maintenance of anesthesia. The pupils are widely dilated and the globe is fixed in position. The twitching spreads to the muscles of the neck, shoulders and arms, finally to the legs and abdomen. As the twitching spreads it becomes more active. Finally violent and sustained epileptiform convulsions occur, associated with cyanosis of varying degree. Administration of oxygen, even under pressure, often fails to alleviate the cyanosis of the extremities. Hyperpyrexia develops and some authorities maintain that this sign must be present if the untoward reaction is to be considered typical. Deepening of the anesthesia does not usually relieve the condition. Following cessation of administration, recovery from anesthesia is delayed. Recurrence of convulsions later, when the patient is in bed has been noted. Death may occur while the patient is in the operating room or later from exhaustion associated with deficient oxygenation. The convulsive seizures may disappear but

* After September 1, 1936, chief anesthetist, Hartford Hospital, Hartford, Connecticut.

the patient may fail to regain consciousness. Death may supervene within three to five days with bronchopneumonia as the salient feature. Weber reported one case in which a child two years of age, failed properly to regain consciousness; when the patient was seen two years later idiocy of the severest grade had developed.

The factors ascribed as causes of these untoward manifestations are numerous and the treatment advised varies with the author's conception of the cause. Wilson and others[18,25,26,74,81,84] were of the opinion that the convulsions were toxic in origin and that acetaldehyde and peroxides in the ether were the offending agents. Gwathmey disagreed with this opinion and presented some experimental evidence to show that lack of adequate preliminary medication was a factor. Hornabrook took the position that atropine was responsible for the untoward reaction but Sington cited his experience at the Hospital for Sick Children, London, where no convulsions had been observed during two years when the total dosage of atropine for all children more than six years of age was 1/80 grain (0.0008 gm.) administered by mouth. Dickson had no doubt in his mind that in his case the convulsions were caused by concentrated ether and an excess of carbon dioxide. Hewer[34] presented arguments to refute Dickson's stand.

Fairlie,[23] although he had never seen a case, hazarded the opinion that there might be something inherent in the superheating of ether when it is given by the Pinson bomb method. Pinson pointed out that convulsions had occurred when the bomb method had not been employed and held to his original suggestion that they are "the outcome of the extensive action of carbon dioxide in patients who are sensitive to this naturally . . . and who are under the influence of ether." McDonagh wrote, "it would appear the anesthetic substances act by subjecting protein particles in the plasma to sudden dehydration and then to an equally sudden hydration . . . the actual state in which the patient's protein particles happen to be before the anesthetic is administered must play a greater part in the production of toxic symptoms." Too deep etherization has been suggested as a cause.[7,10,11,15,18] Hadfield[29] suggested that heat, sepsis or other toxemia, impurities in the ether, and youth might be accessory factors to an unexplained tendency of development of convulsions, but he could not explain absence of record of such cases previous to about 1926. Rood and Webber stated that impurities in the ether might have increased of late, owing to the widespread use of various machines in which fresh supplies of ether are likely to be added to old residues. McDonald and Sapwell each was of the opinion that overoxygenation was not a cause of convulsions, and in this opinion they differed from Mennell. Smith[71] offered the opinion that analysis of the oxygen supply in these cases might provide a clue to the discovery of the cause of this condition. MacKenzie[43] expressed the belief that three factors call for careful consideration: (1) impurities of ether; (2) carbon dioxide imbalance, and (3) acute suppuration[11] or toxemia.[56] Simon[69] was of the opinion that "the septic element is very much to blame." Thomas[77] and Pinson[54] expressed the belief that late ether convulsions could be avoided by careful[5] and judicious administration. Fraser suggested that ketosis was probably a factor. Clarke advanced the hypothesis that "increased vascularity of the cortex cerebri, more particularly of the Rolandic area, produced by a histamine effect, is the underlying cause." Haworth[31] was inclined to think that toxemia and instability of the nervous system are the most probable causes of the condition.

Daly,[19] Sykes[74] and Dawkins each reported one case in which convulsions ceased when the head was raised, suggesting that congestion of the brain had been present. Haworth[31] reported cessation of convulsions after the foot of the bed had been well raised. Courts asked whether "spontaneous overbreathing tetany" might not be a factor. Kemp stated that

"theoretical and practical treatment of ether convulsions indicates that acapnia or carbon dioxide deficit is the causative factor in many instances." Sears suggested that hypoglycemia might be a cause. Waldbott, following a study of 34 cases of "thymic death," suggested that local and general anesthetics may be the source of allergic anaphylactic symptoms. Smith[72] ventured the explanation that heat stroke might have been a factor in the case reported by Wright,[87] who was able to control the muscular spasm below the costal margin by means of spinal anesthesia. Later the same patient was given 3 grains (0.2 gm.) of pentobarbital sodium in 10 per cent solution, with complete cessation of convulsions. The patient's temperature at the time of administration was 106.8°F. The barbiturates are well known to be sedative in action on the heat regulating center. Riddell asked, "may not the cause lie in the three factors—susceptibility, ether vapour, oxygen above the content of atmospheric air?" Rovenstine, in reporting a case of convulsions during ether anesthesia, gave his view that convulsions may sometimes be attributable to trauma. Smith,[73] in commenting on a case reported by Willway, was of the opinion that the muscular spasms were attributable to ethyl chloride.

Since 1929 one of us (Tovell) has taken a keen interest in reports appearing in the literature from time to time regarding "ether convulsions." In January, 1932, his interest was thoroughly aroused when he observed a patient suffering from generalized convulsions (Case 1) which developed in the course of an operation for removal of an acutely inflamed, ruptured appendix.

REPORT OF CASES

Case 1. The boy, aged fifteen years, had been given morphine grain 1/8 (0.008 gm.) and atropine grain 1/200 (0.0003 gm.). Induction was with nitrous oxide and oxygen and ethylene and ether vapor was added. The typical convulsions associated with a marked rise in temperature appeared during the operation and continued to a fatal termination within two hours, in spite of all treatment. The ether was examined and the sample did not contain aldehydes in excessive amounts. Gases from the same tanks had been administered to other patients. Postmortem examination failed to reveal definite evidence of the cause of death. It was noteworthy, however, that pulmonary edema was not present.

Case 11. April 18, 1933, one of us (Tovell) was called to see a girl, aged eight years, who three hours earlier had undergone an operation for the removal of an acutely inflamed, gangrenous appendix. The history revealed that nitrous oxide-oxygen and ether had been employed following preliminary medication with codeine grain 1/2 (0.032 gm.) and atropine grain 1/150 (0.0004 gm.). Generalized convulsions developed in the course of the operation but ceased before the operation was completed. One-half hour after operation the patient's rectal temperature was 105°F. Fifty minutes after operation, muscular spasms developed again and appeared intermittently, with increasing severity, during the next two hours. At this time the patient was conscious. During a seizure the pupils were widely dilated. The general expression was one of extreme fear. A whimpering cry was emitted. The bedclothes were clutched as if in an attempt to control the jactitations. The fingernails and toenails were cyanotic but the lips remained of good color. Sodium amytal grains 10 (0.65 gm.), in 10 per cent solution, was administered intravenously. The convulsions were controlled and did not recur. Recovery was uneventful. The mother said that the child had never had convulsions previously. A sample of the ether used was examined but definite conclusions regarding the cause of the convulsions could not be formulated.

Case 111. In April, 1934, a woman, aged twenty-one years, presented herself for removal of an "interval appendix." She gave a history of having had pain in the lower right abdominal quadrant three months previously; at that time the diagnosis had been appendicitis. Physical examination gave negative results. The systolic blood pressure was 90 mm. of mercury and the diastolic, 68. Preliminary medication consisted of atropine sulphate grain 1/150 (0.0004 gm.) and pentobarbital sodium grain 1 1/2 (0.097 gm.). Anesthesia was induced with nitrous

oxide and oxygen. When consciousness had been lost, ethylene was added and was supplemented by ether vapor. Violent and rapidly recurring hiccoughs developed during induction. As anesthesia deepened, the hiccoughs became less violent and the interval between spasms increased, but in spite of the fact that 2 ounces (60 c.c.) of ether had been used, and thus deep anesthesia had been produced, it was impossible to abolish completely this untoward reaction. On the advice of one of us (Tovell) operation was postponed and administration of the anesthetic was discontinued. Oxygen 90 per cent and carbon dioxide 10 per cent were administered freely and as the patient again entered the first stage of anesthesia the hiccoughing ceased and did not reappear. Two days later an appendix which had undergone chronic catarrhal inflammation was removed without untoward event following induction of spinal anesthesia.

The spasms in this case were so violent and they so racked the patient that the possibility of hiccoughs and "late ether convulsions" arising from similar causes was conceived. One of us (Rosenow) was called to see the patient. The patient related that three days previously she had had a violent attack of hiccoughs lasting approximately twenty minutes. Further hiccoughs had not been experienced until general anesthesia had been induced. Swabbings of her nasopharynx were obtained and cultures were made. Results of experimentation will be outlined later.

Case IV. In February, 1936, a girl, three years of age, entered the hospital for emergency treatment. Diagnosis of appendicitis with rupture was made and immediate operation was advised. Atropine sulphate grain $\frac{1}{300}$ (0.0002 gm.) was administered. Following induction of anesthesia with nitrous oxide and oxygen, with some ether added, a small incision was made. The peritoneum was opened and free pus was encountered. Drainage was instituted. As the incision was being closed, twitching of the muscles of the face was noted. Generalized, clonic muscular spasms soon developed. Cyanosis became marked and oxygen was administered while sodium amytal was prepared for intravenous administration. In order to control the convulsions, 4 grains (0.24 gm.) of sodium amytal was given and this was followed by 500 c.c. of a 10 per cent solution of glucose administered during the next three hours. It was then necessary to repeat the dose of sodium amytal to prevent recurrence of generalized spasms. In the meantime the patient's rectal temperature rose to 108°F. Ice bags were applied and the temperature was reduced to 103°F. Cultures from the wound and nasopharynx were made. The patient lived four days, then died without regaining consciousness. Permission for a postmortem examination could not be obtained.

Case V. In July, 1936, appendectomy for an acute purulent appendicitis grade 4 was performed on a woman, nineteen years of age. Preliminary medication consisted of morphine sulphate grain $\frac{1}{6}$ (0.01 gm.) and atropine sulphate grain $\frac{1}{150}$ (0.0004 gm.) administered subcutaneously. Nitrous oxide and oxygen fortified with ether vapor was employed to produce anesthesia. The ether came from a newly opened container. After administration of the anesthetic agents had been discontinued, muscular twitchings of the face and upper extremities appeared and continued for five minutes. Oxygen and carbon dioxide were administered. When the patient was taken to her room the spasms had ceased. Recovery was uneventful. The first two days following operation nasopharyngeal swabbings were made.

Comment on the cases. In all 5 cases, neither the gases nor the ether was found to be at fault. The method of administration was that usually employed.

Experimental Study

The main symptoms and lesions of persistent, epidemic hiccough,[59] persistent sneezing,[62] and different types of encephalitis,[61] have been produced in animals with the living streptococci isolated from atria of infection of the respective patients,[42] with dead streptococci injected in larger amounts, and with filtrates of active cultures.[60] Streptococci isolated in a study of these diseases possessed on isolation "neurotropic" cataphoretic velocity.[64] Highly specific effects also have been noted following intradermal injection of hyperimmune serums prepared with neurotropic and other streptococci,[63] and in precipitin tests made by layering the patient's serum

over the respective hyperimmune horse serums.[63] On the basis of these results it was thought that the muscular spasms neurotropic, whereas the cataphoretic velocity of the streptococcus obtained from the nasopharynx twelve days later was normal (Fig. 1).

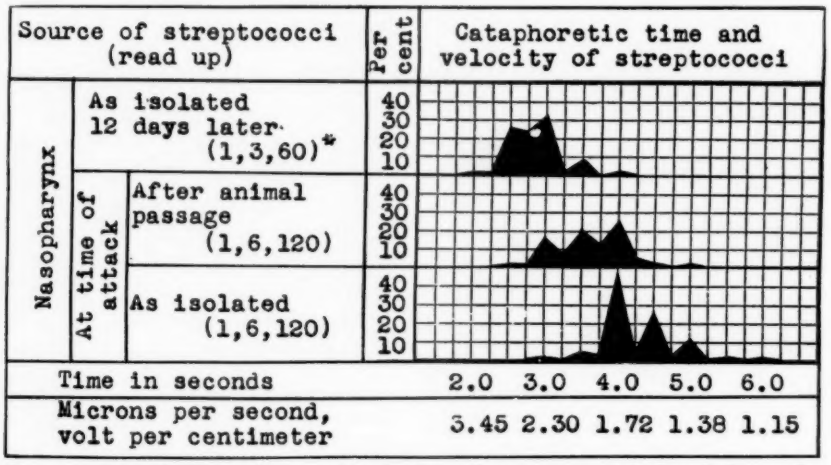


Fig. 1. Cataphoretic time and velocity of streptococci isolated from the nasopharynx of a patient in whom spasms of the diaphragm occurred during nitrous-oxide-ether anesthesia.

* The figures in parenthesis indicate respectively, the number of strains, cultures and streptococci timed.

which sometimes occur in the course of, and following, general anesthesia might be attributable to an unrecognized subinfection by streptococci which had peculiar neurotropic properties. Accordingly, the methods used previously were applied to a study of this perplexing problem.

Case III. The course of events in this case in which the patient had had severe hiccough for a short time three days before severe, uncontrollable hiccough developed in the course of general anesthesia, was especially suggestive of this possibility.

The clear serum obtained from this patient at the time of the attack gave positive precipitin ring tests when layered over the encephalitis and epilepsy antistreptococcus serums. Precipitation did not occur with the poliomyelitis, arthritis, ulcerative colitis and myasthenia gravis antistreptococcus serums, nor with normal horse serum. There was no precipitation between the serum drawn from the patient twelve days later and any of the hyperimmune serums.

The cataphoretic velocity of the streptococcus isolated from the nasopharynx of the patient at the time of the attempted operation when spasms of the diaphragm occurred, and that of the streptococcus isolated from the brain of inoculated rabbits, was markedly

Two rabbits of medium size were given intracerebral injection, one with 0.1 c.c. and the other with 0.3 c.c., of the washings of the nasopharyngeal swabbing of the patient, suspended in 2 c.c. of gelatin Locke's solution. The day after injection, observation of both animals disclosed tremor, increased and jerky respiration, and repeated, clonic spasms of the muscles of the eyelids, ears and abdomen, together with irregular, but sometimes rhythmic, spasms of the diaphragm and paroxysms of sneezing.[62] The tremor and spasms which developed became repeatedly greatly exaggerated and more extensive during induction of, and recovery from, ether anesthesia. The brand of anesthetic ether used throughout this study has a reputation for a high standard of purity. The abnormal reactions occurred equally, whether the ether used was from freshly opened cans, or from cans which had been opened one to several days previously. The rabbit which received the smaller dose died forty-eight hours after injection. Examination revealed moderate, diffuse congestion of the cerebral cortex, marked congestion surrounding the roots of the cervical nerves and a sharply circumscribed region of infiltration and edema of the pia over the anterior aspect of the medulla. Unusually extensive postmortem digestion of the stomach was noted. The cerebrospinal fluid was slightly cloudy.

Cultures from pipettings from the brain yielded a pure growth of the streptococcus; those from the blood proved sterile. The other rabbit

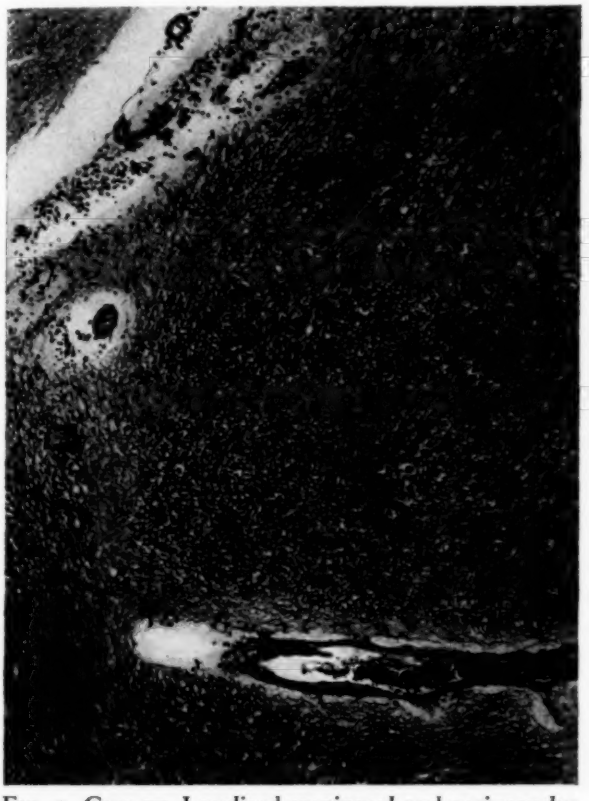


Fig. 2. Case III. Localized meningeal and perivascular infiltration with leucocytes and round cells at the base of the brain of a rabbit forty-eight hours after intracerebral injection of the heat killed streptococcus, after one animal passage. Hematoxylin and eosin, × 75.

recovered.

Two rabbits were given intravenous injection of 12 c.c. of the dextrose-brain broth culture of the streptococcus obtained from the nasopharynx; the microörganism was in the second culture generation. Both rabbits were well the following day. Ether anesthesia had no effect on one, but it caused clonic spasms of muscles of the thorax and diaphragm of the other on two occasions. Sodium amytal, 0.4 c.c. of a 10 per cent solution, injected intravenously, caused the spasms of muscles of the thorax and diaphragm to disappear but incited temporary horizontal nystagmus in both rabbits. The animal that reacted negatively to ether anesthesia was given intracerebral injection, forty-eight hours after intravenous injection, of 2 c.c. of a suspension of the heat killed streptococci equivalent in density to that of a dextrose-brain broth culture. Tremor and clonic spasms of skeletal muscles developed; moreover, there were occasional spasms of the diaphragm, which disappeared following intravenous in-

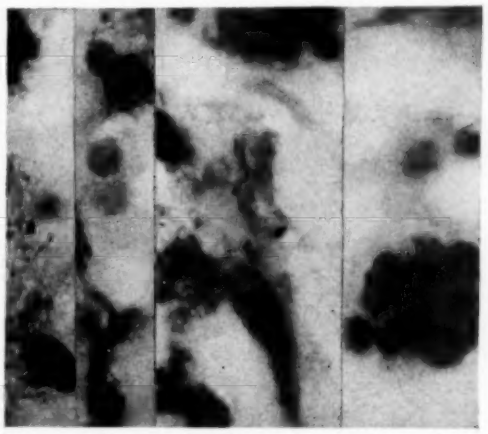


Fig. 3. Case III. Diplococci in lesions of the brain of the rabbit referred to in Figure 2. Modified gram stain, × 1000.

jection of 0.4 c.c. of a 10 per cent solution of sodium amytal. The spasms did not return as the animal recovered from prolonged effects of sodium amytal but ether anesthesia again caused clonic spasms of muscles of the face, eyes, neck, shoulders and thorax. The rabbit was chloroformed twenty-four hours after the intracerebral injection. The cerebrospinal fluid was slightly cloudy and greatly increased in amount. There was moderate congestion of the brain but no lesions of other viscera were seen. Cultures from the brain and blood remained negative. Sections of the brain and medulla revealed slight edema and cellular infiltration of the meninges in sulci and surrounding blood vessels (Fig. 2); also diplococci, free and within leucocytes, were present in the lesions (Fig. 3).

Two additional rabbits were given injection, at 10:00 A.M., April 25, 1934, with the heat killed streptococcus from the primary culture in dextrose-brain broth of the pipettings from the brain of the rabbit that succumbed to intracerebral injection of the streptococcus. One was given 2 c.c. intracerebrally and one 40 c.c. intravenously, of a suspension of the heat killed streptococci equal in density to that of a dextrose-brain broth culture. At 9 P.M., observation of the rabbit that had received intracerebral injection disclosed tremor of the masseter muscles and clonic spasms of the abdominal muscles and diaphragm. Inhalation of ether, on four occasions on the following day, incited extensive spasms of muscles,

including the diaphragm, and on three occasions respiration ceased suddenly, necessitating artificial respiration. The animal was chloroformed forty-eight hours after injection. Sections of the medulla revealed slight infiltration, chiefly by round cells, especially in the anterior aspect of the medulla (Fig. 4), and in sulci of the cerebrum; a few diplococci were found in the lesions.

FIG. 4. Case III. Round cell infiltration in the anterior aspect of the medulla of a rabbit killed two days after intracerebral injection of the heat killed streptococci. Hematoxylin and eosin, × 75.

On April 26, the rabbit that had received intravenous injection appeared to be well. It took ether normally but as it recovered from the anesthetic it licked its mouth and other objects vigorously, and had sharp tremor and spasms of the muscles of the jaw. The licking action and tremor continued for forty-five minutes. These symptoms reappeared in the course of each of six times that anesthesia was effected by ether on the same and on the following day; on one occasion generalized convulsions occurred as the rabbit was recovering from the effects of the ether.

Two rabbits were given injections on April 25, 1934, of a freshly prepared filtrate of the twenty-four hour dextrose-brain broth culture of the streptococcus obtained from the brain of a rabbit that had succumbed to an intracerebral injection of the streptococcus. One was given 2 c.c. intracerebrally; the other, 40 c.c. intravenously. Tremor and spasms of muscles, including the diaphragm, developed in both instances. These symptoms were greatly exaggerated by administration of ether.

Three rabbits were given injections with the streptococcus obtained from the nasopharynx twelve days after the attempted operation. All remained well and reacted normally to ether on repeated tests. They were etherized to death on the fourth day following injection. Lesions were not found and cultures from blood and brain proved negative.

FIG. 5. Case V. Leucocytic and round cell infiltration of the meninges and adjacent brain substance in sulci. The section is of the cerebral cortex of a rabbit that received intracerebral injection of living streptococci. Hematoxylin and eosin, × 1000.

COMMENT. Irregular, greatly exaggerated, spasmodic respirations, associated with spasms of muscles, including the diaphragm, were produced, in varying degrees of severity, in 7 of 8 rabbits which were given injections of streptococci isolated at the time of the attack in Case III. Sensitiveness to ether, in which the muscular spasms were aggravated, was observed in experiments on all the rabbits. These symptoms were not displayed by any of the 3 rabbits which received injections of material obtained from the patient twelve days later.

CASE IV. The cataphoretic velocity of the streptococcus obtained from the nasopharynx of this patient, grown in dextrose-brain broth, was moderately neurotropic. Two rabbits were

given injections, one intravenously with 25 c.c.; the other, intracerebrally with 0.1 c.c. of this culture. In the muscles of the jaws, the ears, and the shoulders of both were observed tremor and spasms which became more marked and more widespread during ether anesthesia.

The former rabbit died thirty hours after injection. The brain was congested. The appendix was swollen and there were a number of hemorrhages in its distal third. A green producing streptococcus was isolated in pure culture from the blood and brain. Observation of the rabbit which received intracerebral injection disclosed, the day after injection, marked tremor, ataxia and clonic spasms of muscles, chiefly of the jaws, the ears, the neck and the shoulders. There was no weakness. The animal was etherized. Excitation and increase in severity and extent of spasms occurred soon after the animal had been placed in the etherizing chamber. Its respiration grew jerky and irregular when under light anesthesia but respiration grew regular and all spasms disappeared when under deep anesthesia. After administration of ether had been discontinued, spasms of muscles returned and horizontal nystagmus developed for a short time and then disappeared. The animal was found dead the following morning. Marked congestion of the brain, and slightly turbid spinal fluid, were found. There were no lesions of the viscera. Cultures from pipettings from the brain yielded large numbers of green-producing colonies of streptococci. Cultures of the blood remained sterile.

COMMENT. Observation of both of two rabbits that were given injections disclosed muscular spasms which became more marked and widespread during induction of, and recovery from, anesthesia. In addition, in the appendix of the rabbit which received intravenous injection, hemorrhages were noted.

CASE V. Observation of all of the 3 rabbits which received injections of the streptococcus obtained from the nasopharynx of the patient, twenty hours after onset of acute symptoms of appendicitis, revealed increased, jerky respirations, tremor and twitching of the masseter muscles, and spasms of the muscles of the eyes and shoulders. The rabbits died in one to two days and in all appendicitis developed, as was manifested by marked congestion and hemorrhages in the mucous membrane or under the peritoneum, hemorrhagic and edematous lymph nodes at the base and a large amount of muco-

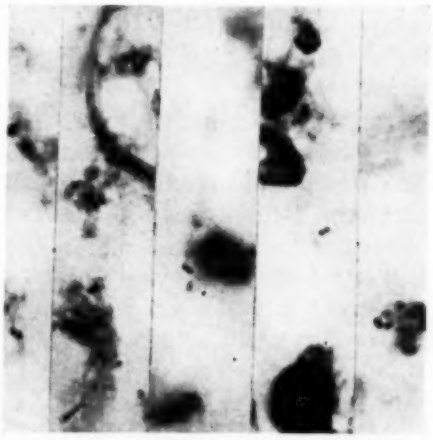


FIG. 6. Case v. Diplococci in lesions of the brain of the rabbit referred to in Figure 5. Brown-Gram stain, × 1000.

purulent material within the lumen of the appendix. All revealed moderate congestion of the brain. One of these rabbits had received intracerebral injection of 0.1 c.c. of the suspension in gelatin Locke's solution; one had received intracerebral injection of 0.1 c.c. of a 1:1000 dilution of the primary culture in dextrose-brain broth, and one had received intravenous injection of 6 c.c. of the primary culture. None of these rabbits was given ether. In examination of the rabbit which had received intravenous injection, in addition to appendicitis, an acute intussusception of the lower part of the ileum and hemorrhages in the colon were found. Cultures from the brains of the 2 rabbits which had received intracerebral injection yielded pure growths of green producing streptococci; those from the wall of the appendix yielded streptococci and gram negative and gram positive bacilli. The blood of both proved sterile, whereas the blood of the animal that had been given intravenous injection yielded a pure culture of the streptococcus. Sections of the brain revealed localized infiltration of the pia and adjacent brain substance, especially in sulci over the cerebral cortex (Fig. 5); diplococci were found in the lesions (Fig. 6).

The primary culture of the streptococcus that was isolated from the brain of the rabbits which had received intracerebral injection was injected intravenously into one rabbit. The animal appeared well forty-eight hours following injection, when it was killed. Examination

revealed congestion of the appendix, small hemorrhages in the mucous membrane of the stomach, one large hemorrhagic ulcer with necrotic walls in the pyloric end of the stomach and hemorrhage of muscle and ligaments surrounding the left knee joint. Cultures from the blood proved sterile.

Three rabbits were similarly given injections, two intracerebrally and one intravenously, with the streptococcus obtained from the nasopharynx of this patient forty hours after onset of the attack of appendicitis. The rabbit which was given intravenous injection was apparently well forty-eight hours after injection but the action of the heart had become irregular and at times about a fourth as rapid as normal. It was not sensitive to ether and was etherized to death forty-eight hours after injection. Lesions were not found in the appendix or intestines. One small hemorrhage was found in the pyloric end of the stomach. Large hemorrhages were found at the base of the posterior leaflet of the tricuspid valve and in the septal wall, just beneath the aortic valves. Cultures from the blood revealed a pure growth of the green producing streptococcus.

The effect of ether was tested on the 2 rabbits which had been given intracerebral injection with the suspension of the nasopharyngeal swabbing made forty hours after onset of symptoms. Both had become hyperirritable and excitable twenty-four hours following injection and one had repeated, mild, muscular spasms in addition. In both, muscular spasms developed or increased during and following repeated ether anesthesia. One died in the course of generalized convulsions following only partial anesthesia, despite the fact that great care was used in the administration of the anesthetic.

The serum of the patient, obtained twenty hours after onset of the attack, gave a positive preciptin ring when the serum was layered over the hyperimmune serums prepared with streptococci isolated in studies of encephalitis and epilepsy, whereas the serum obtained six days after recovery did not give precipitation with any of the hyperimmune serums.

The streptococcus isolated from the nasopharynx twenty and forty hours after onset of the attack, and from the brain and blood of positive animals, was agglutinated specifically by the serum obtained from the patient on the sixth day after onset of symptoms, but not by serum obtained twenty hours after onset of symptoms.

COMMENT. Of 7 rabbits which were given injections of material from the patient, in 5 lesions developed in the appendix and in 2 hemorrhages and ulcer of the stomach developed. Observation of one rabbit which received intravenous injection of the strain obtained two days after onset of the attack disclosed irregularity of the action of the heart; moreover, there were hemorrhagic lesions at the base of the tricuspid and aortic valves and in the septal wall in, or adjacent to, the bundle of His. Observation of both of 2 rabbits which were given injections of the streptococcus obtained from the nasopharynx on the second day of the attack, the 2 rabbits on which the effect of ether was tested, disclosed muscular spasms during etherization and when the animals were recovering from the effects of the ether.

CONTROL EXPERIMENTS

Seventeen rabbits were given injections of streptococci from the nasopharynges of patients used as controls. Two of these patients had acute appendicitis, but spasms did not develop during or following general ether anesthesia; two had ulcers of the duodenum; two, arthritis and fibrositis; one each had rheumatic fever, epidemic vertigo, pyelonephritis, perineuritis, epidemic sore throat and bronchitis. All of these rabbits reacted normally to ether except the one which had received injection of the culture of the streptococcus obtained from the patient who had sore throat and bronchitis. Respirations of this animal became jerky and increased in rate and amplitude; there were tremor and twitching of muscles, clonic spasms of the muscles of the thorax and rapid, vertical nystagmus and blephorospasm. These signs appeared during two inductions of ether anesthesia. At necropsy the lesions in the rabbits injected as controls were characteristic, in important respects, of those of the respective patients from whom

the streptococci had been obtained. Thus, all of 4 rabbits that were given injections of the streptococcus from the nasopharynx of the 2 patients with acute appendicitis, and who reacted normally to ether anesthesia, revealed cloudy swelling and congestion of the entire intestinal tract. In addition, 2 revealed hemorrhages of the transverse colon and appendix, the thymus, and in mesenteric, axillary and popliteal lymph glands. Hemorrhages and ulcer of the stomach or duodenum were found in examination of the 4 rabbits which received injections of the streptococcus obtained from the 2 patients who had duodenal ulcer; hemorrhage, edema and areas of focal necrosis of muscle fibers were found in the animal which had been given injection of the streptococcus obtained from the patient who had rheumatic fever; hemorrhages of muscles surrounding nerves and of fascial sheaths surrounding joints were found in the 3 rabbits which were given injections of the streptococcus obtained from the 2 patients who had arthritis and fibrositis. Aside from congestion of the brain, no lesions were found in the rabbit which had been given injection of the streptococcus obtained from the patient with epidemic vertigo. Hemorrhagic and necrotic lesions were found in the medulla of the kidneys in the 2 rabbits which were given injections of the streptococcus obtained from the patient who had pyelonephritis. Hemorrhagic infiltration and edema of the nerves, nerve sheaths and surrounding fascia were found in the rabbit which had been given intravenous injection of the streptococcus obtained from the tonsils of the patient who had symptoms of acute perineuritis. Hemorrhagic edema and emphysema of the lungs, with rupture of the lung and resulting hemorrhage in the pleural cavity, were found in the rabbit which received intracerebral injection of the streptococcus obtained from the patient who had sore throat and bronchitis.

COMMENT AND CONCLUSIONS

The conditions of the patients studied were closely simulated in animals, both as regards systemic lesions and peculiar reaction to ether anesthesia. Spasms of the diaphragm and "ether convulsions" were reproduced but systemic lesions were absent in the case of hiccough and concomitantly in the rabbits which received injections. In the 2 cases in which the patients had acute appendicitis, and ether convulsions, lesions of the appendix as well as ether convulsions were reproduced in the rabbits. The respective systemic lesions of the control group of patients were also reproduced in animals, but the animals did not manifest abnormal reactions to ether. Antibodies specific for the respective streptococci were demonstrated in the serum of patients after recovery.

Ether anesthesia caused muscular spasms and generalized convulsions of animals which were given injections of streptococci isolated from the patients at the time of the attacks, but not when the streptococci were obtained from the patients after recovery. This peculiar reaction to ether was manifested by some of the animals that at no time before had had spasms. If animals had manifested spasms they were made worse and more extensive by inhalation of ether. Ether also caused spasms to recur soon after apparent recovery from the effects of the streptococcus, but the induced sensitiveness to ether disappeared as recovery became complete.

The symptoms manifested in the course of ether anesthesia by the animals which received injection were similar to those noted in cases of "ether convulsion" that have been reported. Respiration became rapid, jerky and labored and often ceased suddenly, despite great care in the administration of ether. Resuscitation was always difficult and sometimes impossible. Tremor, twitching, and spasms of muscles, of the animals as of the patients, most often began in the muscles of the jaws and face, then tended to spread to the muscles of the neck, shoulders and fore and hind extremities. These manifestations often became worse as they spread and sometimes fatal convulsions developed in the course of, soon after, or late after anes-

thesia. As with patients, so with animals, deepening the ether anesthesia did not always relieve the spasms, whereas intravenous injection of sodium amytal did relieve them. The specific properties of the streptococcus isolated from the throats of patients at the time of the attack, and from the brains of animals which manifested the symptoms and which died, were highly labile. Only freshly isolated strains sufficed to produce highly specific effects.

The results of these experiments suggest that "ether convulsions" are attributable to a neurotoxin or poison produced by some strains of streptococci in amounts insufficient to cause spasms in the absence of anesthesia but which in the course of general anesthesia suffices to incite the muscular spasms characteristic of this condition. It is suggested, on the basis of clinical and experimental evidence, that the barbiturates, administered intravenously, be used to control the muscular spasms, thus permitting subsequent symptomatic treatment.

REFERENCES

1. Anderson, W. D. Ether clonus. *Lancet*, 2: 949–950 (Dec. 22) 1917.
2. Ashworth, H. K. Ether convulsions. *Brit. Med. Jour.*, 1: 851 (Apr. 20) 1935.
3. Baker, A. DeW. Ether clonus. *Lancet*, 1: 35 (Jan. 5) 1918.
4. Bashall, C. J. Convulsions during ether anaesthesia. *Brit. Med. Jour.*, 2: 400 (Aug. 29) 1931.
5. Bashall, C. J. Convulsions during ether anaesthesia. *Brit. Med. Jour.*, 2: 513 (Sept. 12) 1931.
6. Blomfield, J. E. Anaesthetics in Practice and Theory. Chicago, Chicago Medical Book Company, 1923, p. 144.
7. Blomfield, J. Convulsions during general anaesthesia. *Brit. Med. Jour.*, 1: 1095 (June 20) 1931.
8. Bowman, F. H. Convulsions under deep anesthesia. *Am. Jour. Surg.*, 23: 295–296 (Feb.) 1934.
9. Boyle, H. E. G. "Ether clonus": aldehyde and peroxide. *Brit. Med. Jour.*, 2: 566 (Sept. 24) 1927.
10. Boyle, H. E. G. Discussion on late ether convulsions. *Proc. Roy. Soc. Med.*, 21: 1705, 1928.
11. Boyle, H. E. G. Ether convulsions. *Brit. Med. Jour.*, 2: 1009 (Nov. 28) 1931.
12. Brown, D. M. A case of convulsions after ether anaesthesia. *Brit. Med. Jour.* (Clinical Memoranda), 1: 579 (Mar. 31) 1934.
13. Bull, L. J. F. Convulsions occurring during surgical anaesthesia. *Brit. Med. Jour.*, 2: 471 (Sept. 10) 1927.
14. Clarke, L. T. Convulsions during ether anaesthesia. *Brit. Med. Jour.*, 2: 358 (Aug. 22) 1931.
15. Cook, B. E. Ether convulsions. *Brit. Med. Jour.*, 2: 679 (Oct. 10) 1931.
16. Corfield, Charles. Ether convulsions. *Brit. Med. Jour.*, 1: 1052 (May 18) 1935.
17. Courts, A. C. S. Ether convulsions. *Brit. Med. Jour.*, 1: 959 (May 21) 1932.
18. Daly, Ashley. Discussion on late ether convulsions. *Proc. Roy. Soc. Med.*, 21: 1704–1705, 1928.
19. Daly, Ashley. Ether convulsions: a note as to treatment. *Brit. Jour. Anaesthesia*, 9: 67–68 (Jan.) 1932.
20. Dawkins, C. J. M. Ether convulsions. *Brit. Med. Jour.*, 2: 792 (Oct. 27) 1934.
21. Dickson, D. C. Convulsions during anaesthesia. *Brit. Med. Jour.*, 2: 613 (Oct. 1) 1927.
22. Evans, T. J. Ether convulsions. *Brit. Med. Jour.*, 2: 81 (July 12) 1930.
23. Fairlie, H. P. Convulsions during anaesthesia. *Brit. Med. Jour.*, 2: 703 (Oct. 15) 1927.
24. Fairlie, H. P. Convulsions during general anaesthesia. *Brit. Med. Jour.*, 2: 897 (Nov. 12) 1927.
25. Fairlie, H. P. Ether convulsions. *Brit. Med. Jour.*, 1: 1195 (June 28) 1930.
26. Featherstone, Henry. Discussion on late ether convulsions. *Proc. Roy. Soc. Med.*, 21: 1706, 1928.
27. Fraser, Louise. Convulsions during surgical anaesthesia. *Brit. Med. Jour.*, 1: 562 (Mar. 28) 1931.
28. Gwathmey, J. T. Ether convulsions. *Lancet*, 1: 1369 (June 25) 1927.
29. Hadfield, C. F. Discussion on late ether convulsions. *Proc. Roy. Soc. Med.*, 21: 1699–1700, 1928.
30. Hadfield, C. F. Practical Anaesthetics for the Student and General Practitioner. Ed. 2, New York, William Wood and Company, 1931, pp. 111–112.
31. Haworth, James. Convulsions during ether anaesthesia. *Brit. Med. Jour.*, 2: 400 (Aug. 29) 1931.
32. Haworth, James. Convulsions during ether anaesthesia. *Brit. Med. Jour.*, 2: 587 (Sept. 26) 1901.
33. Haworth, James. Ether convulsions. *Brit. Med. Jour.*, 1: 1156 (June 18) 1932.
34. Hewer, C. L. Convulsions during anaesthesia. *Brit. Med. Jour.*, 2: 703 (Oct. 15) 1927.
35. Hewer, C. L. Ether convulsions. *Brit. Med. Jour.*, 2: 80–81 (July 12) 1930.
36. Hewer, C. L. Recent Advances in Anaesthesia and Analgesia. Philadelphia, P. Blakiston's Son and Company, Inc., 1932, p. 41.
37. Holroyd, J. B. H. Ether clonus. *Lancet*, 1: 618 (Apr. 27) 1918.
38. Hornabrook, R. W. Convulsions occurring during surgical anaesthesia. *Brit. Med. Jour.*, 2: 471 (Sept. 10) 1927.
39. Humphrey, George. Quoted by Anderson, W. D. Ether clonus. *Lancet*, 2: 949–950 (Dec. 22) 1917.
40. Kemp, W. N. Tetany during ether anesthesia. *Current Res. Anesth. and Anal.*, 12: 1–4 (Jan.-Feb.) 1933.
41. King, H. J. Convulsions under ether anesthesia. *Am. Jour. Surg.*, 30: 182–184 (Oct.) 1935.
42. Lundy, J. S. Inhalation anesthesia. *Med. Rec. and Ann.*, 23: 1–3 (May) 1936.
43. MacKenzie, J. R. Convulsions during surgical anesthesia. Notes on a series of cases. *Brit. Med. Jour.*, 1: 440–442 (Mar. 14) 1931.

44. MacKenzie, J. R. Convulsions during surgical anaesthesia. *Brit. Med. Jour.*, 1: 685 (Apr. 18) 1931.
45. McDonagh, J. E. R. Convulsions during general and local anaesthesia. *Brit. Med. Jour.*, 2: 1118–1119 (Dec. 10) 1927.
46. McDonald, Niel. Discussion on late ether convulsions. *Proc. Roy. Soc. Med.*, 21: pt. 2, 1706, 1928.
47. Mennell, Z. Discussion on late ether convulsions. *Proc. Roy. Soc. Med.*, 21: pt. 2, 1705, 1928.
48. Muskens, L. J. J. Convulsions during general anaesthesia. *Brit. Med. Jour.*, 2: 897 (Nov. 12) 1927.
49. Mytinger, W. H. Anesthesia in epilepsy. *Am. Jour. Surg.*, 30: 109–111 (Oct.) 1916; *Lancet Clinic*, 116: 317–319 (Sept. 30) 1916.
50. Nosworthy, M. D. The Theory and Practice of Anaesthesia. London, Hutchinson Scientific, 1935, pp. 68–69.
51. Patch, H. H. L. Notes of two cases of epileptiform convulsions during anaesthesia. *Lancet*, 2: 813 (Oct. 14) 1922.
52. Pinson, K. B. Convulsions occurring during surgical anaesthesia. *Brit. Med. Jour.*, 1: 956–958 (May 28) 1927.
53. Pinson, K. B. Convulsions during general anaesthesia. *Brit. Med. Jour.*, 2: 806 (Oct. 29) 1927.
54. Pinson, K. B. General convulsions under ether. *Brit. Med. Jour.*, 2: 277 (Aug. 10) 1929.
55. Pinson, K. B. Ether convulsions. *Brit. Med. Jour.*, 2: 41–42 (July 5) 1930.
56. Priest, W. M. Convulsions during ether anaesthesia. *Brit. Med. Jour.*, 2: 275–276 (Aug. 8) 1931.
57. Riddell, L. A. Ether convulsions. *Brit. Med. Jour.*, 2: 834 (Nov. 3) 1934.
58. Rood, F. S. and Webber, H. N. Anaesthesia and Anaesthetics. New York, William Wood and Company, 1930, pp. 134–135.
59. Rosenow, E. C. The production of spasms of the diaphragm in animals with a streptococcus from epidemic hiccup. *Jour. Infect. Dis.*, 32: 41–71, 1923.
60. Rosenow, E. C. The production of spasms of the diaphragm in animals by living cultures, filtrates, and the dead streptococcus from epidemic hiccup. *Jour. Infect. Dis.*, 32: 72–94, 1923.
61. Rosenow, E. C. Streptococci in relation to etiology of epidemic encephalitis; experimental results in eighty-one cases. *Jour. Infect. Dis.*, 34: 329–389, 1924.
62. Rosenow, E. C. Specificity of streptococci isolated in studies of diseases of the nervous system. Experimental reproduction of persistent sneezing and convulsions. *Jour. Nerv. and Ment. Dis.*, 81: 138–160 (Feb.) 1935.
63. Rosenow, E. C. and Heilman, F. R. New serologic findings in certain infections of man. Abst. Proc. Am. Assn. of Immunologists. *Jour. Immunol.*, 30: 387 (May) 1936.
64. Rosenow, E. C. and Jensen, L. B. Cataphoretic velocity of streptococci isolated in cases of encephalitis and of other diseases of the nervous system. *Jour. Infect. Dis.*, 52: 167–184 (Mar.-Apr.) 1933.
65. Rovenstine, E. A. Convulsions during ether anesthesia: a case report. *Current Res. Anesth. and Anal.*, 14 : 40–42 (Jan.-Feb.) 1935.
66. Sapwell, J. I. Ether convulsions. *Brit. Med. Jour.*, 2: 42 (July 5) 1930.
67. Sears, J. B. Late ether convulsions. Report of two cases. *J. A. M. A.*, 100: 1150–1152 (Apr. 15) 1933.
68. Shipway, F. E. Discussion on late ether convulsions. *Proc. Roy. Soc. Med.*, 21: pt. 2, 1704, 1928.
69. Simon, Phyllis F. L. Ether convulsions. *Brit. Med. Jour.*, 2: 1159 (Dec. 19) 1931.
70. Sington, Harold. Convulsions during anaesthesia atropine in childhood. *Brit. Med. Jour.*, 2: 566–567 (Sept. 24) 1927.
71. Smith, A. D. J. Ether convulsions. *Brit. Med. Jour.*, 2: 80 (July 12) 1930.
72. Smith, F. W. G. Ether convulsions or heat-stroke? *Brit. Med. Jour.*, 1: 77–78 (Jan. 13) 1934.
73. Smith, P. J. Ether convulsions. *Brit. Med. Jour.*, 1: 901 (Apr. 27) 1935.
74. Sykes, W. S. Ether convulsions. *Brit. Med. Jour.*, 1: 1128–1130 (June 21) 1930.
75. Sykes, W. S. Modern Treatment Anaesthesia. New York, W. W. Norton and Company, Inc., 1932, p. 87.
76. Sykes, W. S. Ether convulsions. *Brit. Med. Jour.*, 2: 610 (Sept. 29) 1934.
77. Thomas, L. K. Discussion on late ether convulsions. *Proc. Roy. Soc. Med.*, 21: pt. 2, 1705, 1928.
78. Vignes, Henri. Ether clonus. *Lancet*, 1: 550 (Apr. 13) 1918.
79. Vignes, Henri. A propos de la note de T. Rietz sur le tremblement pendant l'anesthésis générale. *Compt. rend. Soc. de biol.*, 86: 418–419 (Feb. 25) 1922.
80. Waldbott, G. L. "Late ether convulsions." *J. A. M. A.*, 100: 1557 (May 13) 1933.
81. Walton, A. C. R. A note on ether convulsions. *Brit. Med. Jour.*, 2: 8–9 (July 7) 1928.
82. Weber, F. P. Complete mindlessness (lowest degree of idiocy) and cerebral (cortical) diplegia, after *status convulsivus* associated with ether anaesthesia. *Brit. Jour. Child. Dis.*, 28: 14–21 (Jan.-Mar.) 1931.
83. Willway, F. W. Ether convulsions with normal behaviour durin g subsequent ether anaesthesia. *Brit. Med. Jour.* 1: 764 (Apr. 13) 1935.
84. Wilson, S. R. "Ether" convulsions. *Lancet*, 1: 1117–1119 (May 28) 1927.
85. Wilson, W. S. Convulsions under ether anesthesia. *Current Res. Anesth. and Anal.*, 14: 281–282 (Nov.-Dec.) 1935.
86. Woolmer, R. F. and Taylor, Stephen. Late ether convulsions: a study based on four cases. *Lancet*, 1: 1005–1007 (May 2) 1936.
87. Wright, A. D. Nembutal in ether convulsions. *Brit. Med. Jour.*, 2: 1210–1211 (Dec. 30) 1933.
88. Wright, A. D. Ether convulsions. *Brit. Med. Jour.*, 1: 949 (May 4) 1935.

ANESTHETICS AND LIVER FUNCTION

WESLEY BOURNE, M.D., F.R.C.P. (CAN.)

Lecturer in Anaesthesia, McGill University

MONTREAL

INTEREST in the effects of anesthetics on metabolism has been continual ever since their universal employment, and although that part of the general subject which has to do with their actions on the liver did at first seem separate, in some respects specific, and rather circumscribed, it has become more and more evident that the disturbances which anesthetics cause in the liver take place concurrently and in an interdependent manner with the many others in the rest of the organism. And yet the increasing attention towards the effects of anesthetics on the liver, over those on other structures, has not been altogether irrelevant nor perhaps too immoderate, all the more so, on account of the many vital functions of that great organ.

Casper[1,2] was the first to suggest the possibility of death from the delayed action of chloroform and mentioned Dohlhoff's case of January, 1849, at the Magdeburg hospital. About the same time Langenbeck[3] reported a similar death occurring seventeen hours after operation, in which at autopsy the liver was found to be very fatty. The acute experiments of Nothnagel,[4] done in 1866 on rabbits, show that chloroform as well as ether may produce fatty changes in the liver, heart and kidneys. In 1882 Rosenbaum[5] demonstrated that for a long time after chloroform anesthesia the liver is poor in glycogen. In 1883, Ungar and Junkers[6] found extensive fatty changes in the liver, heart and voluntary muscles in experiments on dogs which were killed forty-eight hours after single administrations of chloroform. After repeated inhalations some of the animals were allowed to die and the lesions in these structures were found to be much more severe and fatty changes were noted as well in the kidney, spleen and mucous membranes of the respiratory and alimentary tracts. They attributed these effects to the direct action of the drug on the tissues. Working independently in 1889 at Berlin, Strassmann[7] and Ostertag[8] confirmed the findings of Ungar and Junkers, and, in addition, the former discovered that chloroform caused an increased excretion of nitrogen in starved animals; while the latter made the important observation that dogs exhibit great individual differences in resistance to chloroform. Thiem and Fischer,[9] in the same year, reported the case of a man who died four days after chloroform anesthesia which was produced for an operation on the knee joint. At necropsy the fatty changes in the liver were very marked while the kidneys seemed normal. These observers then experimented on rabbits and dogs and found that chloroform produced marked fatty changes especially in the liver. One year later Bastianelli[10] published an account of 3 deaths occurring in three to ten days after chloroform narcosis. He could find no other apparent cause for these deaths than the anesthetic. His patients had the typical symptoms of vomiting, icterus, delirium and coma. Autopsy in one of these cases revealed extensive fatty degeneration of the liver and moderate fatty changes in the kidney and heart, as well as subserous hemorrhages.

The first carefully detailed description of the naked eye and microscopical appearances of the changes which may take place in human organs after the inhalation of chloroform, was given by Fraenkel[11] of the new general hospital of Hamburg-Eppendorf in 1892. He studied 5 cases in which chloroform had been used during two to

four hours. The deaths occurred from forty hours to twenty days after the operations. The heart showed marked fatty degeneration in all these cases. In the kidneys there was pronounced degeneration of the epithelium, especially of the convoluted tubules, varying in intensity from cloudy swelling to actual necrosis; in one instance there were considerable fatty changes. Although he laid less stress on the liver effects, he was able to detect a fatty change, especially at the periphery of the lobules, in 4 of the cases. The liver cells were degenerated and their nuclei often necrosed. Deposition of fat was observed also in the voluntary muscles, and in the ascending aorta. After comparing these morbid changes in the parenchymatous organs with those found in patients dying from sepsis and other causes, he came to the conclusion that the former were specific for the action of chloroform. It is of particular interest to quote his reference to a case of a strong muscular man, aged thirty-eight years, who died sixteen days after resection of the pylorus for carcinoma. In spite of the fact that he was kept under chloroform for four hours, the heart, liver and voluntary muscles showed no abnormality, and only a very slight parenchymatous degeneration was present in the kidneys. The patient died of gangrene of the lung. He mentions this case because it seems to support the idea of the importance of idiosyncrasy in chloroform poisoning. We may compare the previously mentioned observation of Ostertag concerning the great individual differences in resistance in dogs to this drug. Fraenkel states that whereas clinical symptoms may be very mild, the autopsy findings may show extreme parenchymatous degenerations.

Several other earlier observers have reported instances of the effects of chloroform on the liver, and it may be stated at once that it is not intended at this time to recount all of their findings, but rather only those which seem primordial in possessing important and pertinent facts. Separately, Bandler,[12] Heintz[13] and Marthen[14] in 1896 recognized necrosis in the livers of fatal cases and produced necrotic lesions in the livers of dogs and rabbits, all from chloroform anesthesia. Bandler refers to many previous authors, and gives the detailed symptoms of an otherwise healthy man who died in Wolfler's clinic in Prague on the fourth day after one hour of chloroform anesthesia for strangulated hernia. Leucine and tyrosine were found in the urine. Microscopically the liver was pervaded with fat and showed a granular detritus in place of the normally outlined cells. In discussing the etiology of this case he excluded sepsis as well as iodoform and sublimate intoxications, and concluded that chloroform was the most likely cause of the damage done. He gives an account of his experiments on rabbits and dogs, from which there was confirmation of the findings of Ungar and Junkers and of Strassmann concerning the action of chloroform on the liver. He administered ether to 4 rabbits and to 4 dogs for relatively long periods and in some instances repeatedly. In only one of these was any action on the liver found; that is, slight fatty changes in a dog after four administrations on successive days.

The clinical accounts of Heintz and Marthen are both very similar to that of Bandler. The former believed that death may not be attributed to functional disturbances of a single organ but rather to an intoxication which produces pathological changes in most of the organs by no means proportionate either to the length of anesthesia or the quantity of chloroform used, and that idiosyncrasy seems to be an important factor. In his description of the liver findings Marthen mentions fatty infiltration at the periphery of the lobules and absence of the nuclei of the cells of the central zones.

Although previously mentioned by Fraenkel, the year 1896 marks the beginning of the recognition of necrosis as the most important of the changes produced by chloroform. Lengemann[15] reported in 1900 from the Surgical Clinic of Mikulicz

and the Pharmacological Institute of Filehne in Breslau that even prolonged ether anesthesia causes no damage to the viscera, i.e., liver, myocardium and kidney, whereas with chloroform no matter what the circumstances the effects are deadly. Both anesthetics were administered in vapour form by a pump and the percentages were measured. Truly the epoch of the "nineties" saw several manifestations of general scientific marvels, to which no other short period can point. The few references which have been given here are illustrative of the many attempts to elucidate the effects of anesthetics during these years.

As time went on these effects were explained in various ways; for example, Guthrie,[16] who gave an excellent description of the symptoms of late chloroform poisoning, claimed that the root of the trouble lies in a preexisting fatty condition of the liver and that the anesthetic acted only as a "last straw." Brewer[17] discussed all the possible causes and concluded that the condition was one of "acetonaemia"; and others, separately, have called it "acid intoxication," "aciduria," and "acute yellow atrophy." Among the earlier observers may be mentioned Stiles and McDonald,[18] who gave a very comprehensive account of delayed chloroform poisoning up to their time (1904), with good references and colored plates showing intense fatty infiltration and central necrosis of the liver lobules of a rabbit and a patient. Another description of the effects of anesthetics on the liver, with which all anesthetists should be familiar, is that given by Bevan and Favill.[19] They recount and discuss the cases from the literature, the symptoms, predisposing causes and pathological findings. In their carefully tabulated conclusions they mention

> . . . a definite symptom-complex which makes its appearance from 10 to 150 hours after anaesthesia. This symptom-complex consists of vomiting, restlessness, delirium, convulsions, coma, Cheyne-Stokes respiration, cyanosis, icterus in varying degree, and usually terminates in death . . . chloroform is the anaesthetic which produces this. Ether is seldom the cause of a death of this kind.

About the same time Doyon and Billet,[20] working in the laboratories of professors Morat and Renaut in Paris, administered chloroform in oil to dogs by stomach tube and found that the lesions of the hepatic cells were principally in the centre of the lobule. They appear in one of three states which seems to constitute the progressive steps of the same process, namely: (1) Hyaline degeneration, the cells are very slightly affected, but there is no reticular structure. The nuclei are healthy. (2) A second stage wherein the protoplasm is fragmented, reduced to granulations (more or less large) and without structure—granular degeneration. (3) A last stage in which the protoplasm does not exist or is reduced to fine, somewhat colored granulations; the nucleus is colored a little and fragmented, indeed it may have completely disappeared—complete necrosis. In general there is marked fatty degeneration. The kidneys show lesions of acute epithelial nephritis.

Wells[21] has propounded the hypothesis that anesthetics, like some other substances, may inhibit the actions of the enzymes which produce oxidations, which maintain the equilibrium between glycogen and sugar, which split fats and probably also synthesise them, and also those which split up proteids. At the same time the action of the autolytic enzymes is not impeded and synthesis ceases while proteolysis continues, hence the process is all in one direction and the cell digests itself until its structure is destroyed and its proteids have broken up into simple nitrogenous substances, such as leucine, tyrosine and ammonia compounds. Such products of disintegration enter the circulation and produce toxic effects, added to which will be the poisonous substances that accumulate because of the impaired function of the degenerated liver and kidney. Presumably the liver is the most affected because it is the site of the most active autolytic and oxidative processes in the

body. In a later paper Wells[22] concludes that there are two types of cases, those in which the effects are principally on the kidney producing symptoms resembling "acidosis" or "acetonaemia," occurring usually in children, and a second group with severe jaundice, seen more frequently in adults, wherein the chief seat of action is the liver.

Against the hypothesis of Wells one finds the results of the work of Howland and Richards[23] on dogs which show that the proportions of nitrogen as urea, ammonia and undetermined compounds, so closely approximated the normal that death could not have been due to the accumulation of amino-acids or to an acid intoxication.

What a prodigious organ is the liver, with its immensity, its 200,000 (Sappey) lobules of beautiful intimate structure, its double blood supply, its bipartite rhythmic activity, and its many vital functions. Yet it is very vulnerable and its cells are exceedingly susceptible to insult, so that in the very performance of their duties they are apt to succumb easily. But they are possessed of remarkable regenerative powers. The regenerative changes in the liver were studied by Podwyssozki[24] fifty years ago in the rat, cat, rabbit and guinea pig. He found that loss of liver substance is repaired by proliferation of the liver cells and the cells of the small bile ducts. Where there is gross injury, an abundant formation of connective tissue occurs as well, and the bile ducts proliferate freely and from them new liver cells may develop. When Podwyssozki had finished his work he noticed that Bizzozero[25] had just published very similar results. Then Ponfick[26] showed that after removal of all but one lobe of the liver in dogs the needs of the organism caused a hypertrophy of the remaining liver substance which resulted from the great multiplication of the liver cells everywhere throughout the lobule and the establishment of newly formed blood capillaries. This work was repeated and verified by von Meister,[27] who states that when four-fifths of the liver of rabbits, rats or dogs, is removed it can regenerate to its usual weight of reconstructed organ parenchyma.

Meder[28] and several others have at different times since shown that similar repair takes place in the liver after intoxications such as "acute yellow atrophy," and Pearce[29] has reported his study based on material from the livers of 16 dogs representing periods varying from thirty-eight hours to thirty-six days after the injection of an hemagglutinative serum which produces necrosis. He gives the details of his findings concerning the regeneration of the liver tissue and states that the most striking feature is the great power of the liver cells to increase by direct division; also, in the late stages of the repair of extensive necrosis many multinucleated liver cells, most of which surround fragments of necrotic cells, may be seen between the normal liver tissue and the dense bands of new tissue. Whipple and Sperry[30] made a careful study of tissue repair in the dog's liver following central necrosis from chloroform anesthesia, and among other conclusions state that if an animal recovers, the repair takes place rapidly and brings the liver back to normal in two to three weeks; also that the pathology of chloroform poisoning is identical in dogs and in man. There have been numerous confirmations of the pathological and regenerative findings following liver damage from various causes.

It is well to remember that Mann and Magath[31] have shown that the experimental production of a chronic functional insufficiency of the liver has been difficult because of the enormous regenerative power of-the organ. It is possible to remove all of the liver of the dog except the two lower right lobes (approximately 70 per cent) without serious damage to the portal and vena cava circulation; the animals do not seem to suffer from such loss. The reason for this may readily be ascertained by examination a few months after operation, when the two remaining lobes will be

enlarged and the amount of tissue practically the same as before operation.

At this juncture it is worthy of note that Williamson and Mann[32] have shown that the characteristic symptoms which follow hepatectomy are not observed after poisoning with chloroform or phosphorus, although the results of the poisoning are in many instances fatal. Hypoglycemia occurred in but a small percentage of their experiments and uric acid in the majority. They state that the results prove conclusively that the poisons, while greatly injuring the functions of the liver, do not produce complete hepatic insufficiency. Other tissues and organs are undoubtedly profoundly affected, and in many instances the functional damage to the liver is probably not the primary cause of death. However valuable the studies on the effect of chloroform, phosphorus and allied poisons may be, particularly relative to hepatic disease, conclusions with regard to the function of the liver based on such studies must be drawn very cautiously.

Despite the profusion of liver regeneration, complete functional recovery is not fully established for some considerable time after the tissue seems to be perfectly normal under the microscope. This has been abundantly proved since the introduction of the dye tests by Abel and Rowntree,[33] who used phenoltetrachlorphthalein. Rowntree, Hurwitz and Bloomfield[34] made a comparative study of all the then known tests for liver function and concluded that this dye test was most reliable and that its employment gave quantitative results. The dye is injected into a vein and recovered quantitatively from the feces to which it is excreted from the liver through the bile. Whipple and Speed[35] found a drop in the fecal output of the dye, some of which is now excreted in the urine, after the administration of chloroform. When ether is given over a period of two hours, this dye test shows a liver function interference which lasts for twenty-four hours. They show that this physiological test is more sensitive than any estimate based on histological evidence. In 1922 Rosenthal[36] modified this test by substituting the measurement of the degree of the retention of the dye in the blood for the study of its excretion in the bile, that is, he measures the rate of its disappearance from the blood. Then Rosenthal and White[37] studied a large group of phthalein dyes and found bromsulphalein to be the most suitable. Normally the liver can remove it almost completely from the blood within fifteen minutes after intravenous injection, but if the liver is injured it cannot normally take up the dye, which therefore remains in the blood for a long time. If 80 per cent of the rabbit's liver is removed and the dye injected, more than 80 per cent of it will still be present in the blood fifteen minutes after injection, at which time it should normally be removed.

Rosenthal and I[38] conducted a series of experiments for the purpose of studying the effect of various anesthetics on the liver, as indicated by bile pigment disturbances and by the bromsulphalein test for hepatic function. The changes which anesthetics produce on the liver, however, have a more general interest in that this impaired function is only a reflection of the widespread depression of cell activity resulting from certain anesthetics; analogous changes are undoubtedly produced in most other organs. We compared the dye test with two others based on pigment metabolism, namely, the bilirubin concentration in the blood and the urobilinogen excretion in the urine; the former by the method of Meulengratsch, the latter by the technique of Wallace and Diamond.[39] It may be said in passing that this bromsulphalein dye test has been very well accepted as being very delicately sensitive and highly specific in detecting injury to the liver, especially that kind which is at present under consideration.[40–42, et al.] We found that half an hour of chloroform anesthesia produced a transient bilirubinemia and urobiligenuria that returned to normal in three days. The bromsulphalein test, however, showed dye retention

for eight days. With two hours of chloroform, the icterus index rose to 11 on the following day and required ten days to return to normal. The urobiligen dilution index in the urine rose from the normal value of 5 to 100 on the following day, and also required ten days for a return to normal values. The bromsulphalein test showed 100 per cent retention of dye in the blood (fifteen minutes after its injection) for the first two days after chloroform and required six weeks for recovery. These observations demonstrate that the dye test affords a much more sensitive index of injury to the liver cells than do estimations of bile pigments in the blood and urine. We stated that chloroform poisoning is synonymous with chloroform anesthesia.

With ether we found that there is always a slight impairment of function as shown by the bromsulphalein test, although no abnormalities in urobilinogen excretion and no increase in bilirubin in the blood occurred. Even half an hour of ether anesthesia produces demonstrable functional impairment with the bromsulphalein test, and longer periods of anesthesia cause proportionally increased degrees of injury. The striking difference between the ether and chloroform results is that with the former the animal has returned to normal the next day, while with chloroform the harm continues to progress and does not reach a maximum until the day after the anesthesia. Our experiments with nitrous oxide, as well as with ethylene, showed that when sufficient oxygen is supplied, anesthesia from one to two hours produced neither immediate nor delayed impairment of hepatic function, whereas when these gases were administered in such a manner that considerable cyanosis was present, we found that all the animals sustained an immediate impairment of function, which did not return to normal the next day as with ether, but required several days for recovery. There was also an increase in the blood bilirubin for two or three days following the experiment. These experiments should teach us very carefully to avoid cyanosis in anesthesia, and it is of interest to note that Koehler, Brunquist and Loevenhart[43] have shown that deliberately produced anoxemia in hogs causes a more marked acidosis than has ever been seen otherwise.

Employing the same bromsulphalein test, the effects of a number of other anesthetics on liver function have been studied from time to time. Amytal,[44] a representative barbiturate, given to dogs in doses from 40 to 60 mg. per Kg. of body weight, producing complete anesthesia, caused very slight dye retention in the blood, and there was no evidence of delayed action. In human cases there was no dye retention following the administration of 1 gram of amytal.

Avertin[45] administered to dogs in doses of 500 mg. per Kg. of body weight produces slight and transient but no delayed liver damage, and in human cases there was no dye retention twenty-four hours after the administration of 100 mg. per Kg. Repeated administration of avertin in normal dogs produces only a mild parenchymatous degeneration of the liver and kidneys,[46] and when the dog's liver is purposely damaged by chloroform, the additional damage done by avertin is slight and varies in proportion to the severity of the damage previously produced by chloroform. This added liver damage disappears within twenty-four to forty-eight hours and does not affect the total period of recovery from chloroform poisoning. Repeated[47,48] administrations of avertin in man—one individual on 22 occasions over a period of less than ten weeks; another, 11 times during sixteen months—were followed by no appreciable liver damage. Kaczander[49] determined the bilirubin content of the blood of 9 subjects before, during and from one to eight days after avertin narcosis, and found in no case any variation from normal limits. He concluded that avertin does not have a toxic action on the liver.

Similarly, vinyl ether[50] has been studied and proved as not altering the liver function appreciably in dogs. In those experi-

ments where cyanosis was a feature of the anesthesia, moderate liver damage occurred, thought to be due to the associated anoxemia. Vinyl ether anesthesia did not enhance the liver function damage produced previously by the inhalation of chloroform, nor does it delay the period of recovery from this damage. At the same time it was found that the effect of vinyl ether anesthesia upon liver function in partially starved dogs is not appreciably different from that produced in normal animals. The bromsulphalein dye test for liver function has been applied in obstetrical anesthesia[51] produced by vinyl ether, a comparison being made with that of chloroform. The dye retention in the chloroform cases indicated definite liver impairment, whereas the administration of vinyl ether under identical circumstances was followed by practically no liver dysfunction.

Goldschmidt, Ravdin and Lucke[52] have made a comparison of the relative incidence of liver necrosis in dogs anesthetised in a semiclosed system, when the anesthetic was volatilized with air and when it was volatilized with oxygen. They showed that the use of oxygen with either vinyl ether or chloroform is a potent factor in the reduction of postanesthetic liver necrosis. With them, vinyl ether did not cause liver necrosis in dogs until the anesthesia was maintained for a three hour period. The incidence of such necrosis was nearly twice as high when the anesthetic was volatilized with air as with oxygen; whereas the incidence of liver necrosis following one hour of chloroform anesthesia was approximately ten times as great when the anesthetic was volatilized with air as with oxygen. Such a recent publication on the beneficial use of oxygen is timely, because it has not been emphasized sufficiently, although some mention sporadically has been made ever since the days of Offergeld,[53] who recommended that the best method of preventing the accidents of delayed chloroform poisoning is the administration of oxygen with the chloroform.

It would seem that cyclopropane anesthesia is absolutely free from the possibility of producing any interference with liver function for the simple reason that an abundance of oxygen is used along with this gas anesthetic. This has been proved by experiments on dogs,[54] the data of which show that cyclopropane anesthesia does not damage the normal liver, even after repeated administrations, or after long periods; that it does not enhance the liver damage purposely produced by chloroform nor impede the usual recovery of the liver from chloroform poisoning, even when the cyclopropane anesthesia is prolonged; and that it does not cause liver impairment in starved dogs, even after a three hour period of anesthesia. Furthermore, the bromsulphalein dye test was carried out in three normal obstetrical cases, and in one of eclampsia.[55] Practically no dye was retained in the blood of the normal women when the test was applied about twenty-four hours after the administration of cyclopropane. As the liver of the eclamptic woman was damaged to an extent of more than 55 per cent before delivery, the damage was not enhanced by cyclopropane, there being less than 50 per cent dye retention in her blood twenty-two hours after anesthesia.

Disturbances in nitrogenous, carbohydrate and fat metabolism by anesthetics have been the subject of numerous investigations ever since the days of Strassmann.[7] There is apt to be a marked increase in protein catabolism and elimination of nitrogen, sulphur and phosphorus compounds. The majority of investigators report hyperglycemia after all forms of narcosis, and Roscher[56] reports its occurrence even after local anesthesia. Naturally increased postoperative blood sugar has been placed in causal relationship with the acidosis of anesthesia and attributed to limitation of oxidation. Roscher shows that ether and chloroform narcosis, and novocaine-adrenalin anesthesia cause a decrease in liver glycogen. It is believed that fat and certain amino-acids give rise to the

production of ketone bodies. In a report on the influence of fasting and various diets on the liver injury effected by chloroform anesthesia, Davis and Whipple[57] state that the degree of chloroform injury seems to depend not only on the amount of chloroform absorbed, but on the subject's nutrition. They offer no adequate explanation for the protective or injurious effects of any diet in modifying the action of chloroform. Carbohydrates build up the liver glycogen. Whatever the protective action may be, it certainly seems to be built up by the body and does not lie in the foods as such. They found that starved animals were very susceptible to liver injury. Sugar and diets rich in carbohydrates, fed in the days preceding chloroform anesthesia, exert a marked protective action against liver injury. Milk, too, affords considerable protection. Davis, Hall and Whipple[58] have shown that the feeding of sugar very materially lessens the urinary nitrogen excretion, and the liver repair is much more rapid. Recently, Renshiro Inami[59] has reported that nitrous oxide, ether and chloroform anesthesias all cause an increased destruction of protein in rabbits, as shown by the increased urine nitrogen and the increased non-protein nitrogen of the blood. The maximum change is obtained in six, four and two hours, respectively; that is, the most toxic drug attains its maximal effect soonest. The degree of narcosis is more important in causing this increased catabolism than is the duration of anesthesia or quantity of material used. He finds that chloroform damages the rabbit's kidney. In his clinical studies he finds very similar effects. These, too, depend upon depth of anesthesia rather than on duration or quantity. Chloroform causes kidney injury in man.

Bollman and Mann[60] have found that after total removal of the liver, uric acid formation in the dog is unimpaired, but the destruction of uric acid and the formation of allantoin are entirely prevented. They had previously stated that the best test of functional deficiency of the liver in the dog which has been found is based on the facts that destruction of uric acid depends on the liver, that this is the most easily injured of the known functions of the liver, and that the amount of uric acid secreted in the urine appears to bear a definite relation to hepatic damage. This test is easily performed by determining the amount of uric acid eliminated in the urine during a standard period of time following the ingestion of a standard meal with a high content of purine. Whether or not such a test will be of value in man remains to be proved.

Finally, in connection with metabolism, it is of exceptional interest to note that recently Forsgren[61] has brought forward the information that in rabbits, and probably also in man, assimilatory processes—glycogen formation, protein, and possibly water retention—occur chiefly during the night, while the secretory processes—bile and urea formation—predominate during the day. It is also supposed that the greatest heat production in the liver occurs during the secretory phase. He discusses the practical significance of this diurnal rhythm.

CONCLUSION

It can be said that, with the exception of cyclopropane, all anesthetics may cause some impairment of liver function. But this should not be taken too seriously, except in the case of chloroform, in view of the facts that nowadays one is able to evaluate surgical risks with excellent precision, there are so many anesthetic agents and methods from which to choose, and we have at our disposal a considerable number of preventative and alleviatory measures, particularly the use of oxygen.

REFERENCES

1. Casper's *Wochenschrift*, 1: 58, 1850.
2. Casper's *Forensic Medicine*, 2: 293–296, 1862.
3. Langenbeck. Behrend's Chloroform Statistik, Hanover, 1850.
4. Nothnagel. (Medicinischen Poliklinik zu Königsberg.) Die fettige Degeneration der Organe bei Aether und Chloroformvergiftung. *Berl. klin. Wchnschr.*, 2: 31–35, 1866.

5. Rosenbaum, F. Untersuchungen über den Kohlehydratbestand des thierischen Organismus nach Vergiftung mit Arsen, Phosphor, Strychnin, Morphin, Chloroform. Dissertation, Dorpat, 1879. *Arcb. f. exp. Patb. u. Pbarmakol.*, 15: 450, 1882.

6. Junkers. Ueber fettige Entartung in folge von Chloroform Inhalationen. Inaug. Diss., Bonn, 1883.

Ungar. Ueber todtliche Nachwirkung der Chloroforminhalation. *Vrtljscbr. f. gericbtl. Med.*, 47: 98, 1887.

7. Strassmann, F. Die todtliche Nachwirkung des Chloroforms. *Virchow's Arcb. f. patb. Anat. u. Pbysiol.*, 115: 1–14, 1889.

8. Ostertag, R. (Städt Thierarzt in Berlin.) Die todtliche Nachwirkung des Chloroforms. *Virchow's Arcb. f. patb. Anat. u. Pbysiol.*, 118: 250–319, 1889.

9. Thiem and Fischer. Ueber todtliche Nachwirkung des Chloroforms. *Deutscb. med. Zeitung*, 10: 1111, 1889.

10. Bastianelli, R. Sulla morte tardiva per chloroformio. Bull. della Soc. Lancisiana deglia Ospedali di Roma, June 22, 1890, p. 325. Abstract in *Rev. de Sciences méd.*, 39: 625, 1892.

11. Fraenkel, Eug. Ueber anatomische Veränderungen durch Chloroformnachwirkung beim Menchen. Aus dem neuen allgemeinen Krankenhause zu Hamburg-Eppendorf. *Virchow's Arcb. f. patb. Anat. u. Pbysiol.*, 127: 381–396, and 129: 254–284, 1892.

12. Bandler, V. (Operationszogling aus der Prager chirurgischen Klinik des Prof. Dr. A. Wölfler.) Ueber den Einfluss der Chloroform- und Aether-Narkose auf die Leber. *Mitt. a. d. Grenzgeb. d. Med. u. Cbir.*, 1: 303, 1896.

13. Heintz. Der protrahirte Chloroform Tod. Inaug. Diss., Rotterdam, 1896.

14. Marthen, G. Ueber Tödliche Chloroform-Nachwirkung. *Berlin. klin. Wcbnscbr.*, 33: 204–207, 1896.

15. Lengemann, P. (Aus der Breslauer chirurgischen Klinik des Prof. Dr. V. Mikulicz und dem pharmakologischen Institut des Prof. Dr. Filehne.) Sind die Schädlichen Nachwirkungen des Chloroforms von der Technik der Narkose abhänzig? *Beitr. z. klin. Cbir.*, 27: 805–828, 1900.

16. Guthrie, Leonard G. (Children's Hospital, Paddington-Green.) On the fatal effects of chloroform on children suffering from a peculiar condition of fatty liver. *Lancet*, 2: 10, 1903.

17. Brewer, George E. Fatal acetonaemia following an operation for acute appendicitis. *Ann. Surg.*, 36: 481–493, 1902.

18. Stiles, Harold J. and McDonald, Stuart. (Royal Edinburgh Hospital for Sick Children.) Delayed chloroform poisoning. *Scot. Med. and Surg. Jour.*, 15: 97–149, 1904.

19. Bevan, A. D. and Favill, H. B. Acid intoxication, and late poisonous effects of anaesthetics—hepatic toxaemia, acute fatty degeneration of the liver following chloroform and ether anaesthesia. *J. A. M. A.*, 45: 691, 1905.

20. Doyon, M. et Billet, J. (Lab. Morat et Renaut.) Rapport entre l'incoagulabilité du sang et les lésions hepatiques dans l'intoxication subaigue par le chloroforme. *Compt.-rend. Soc. de biol.*, 58: 852–853, 1905.

21. Wells, H. Gideon. (Dept. Path., Univ. Chicago.) Delayed chloroform poisoning and allied conditions. *J. A. M. A.*, 46: 341–343, 1906.

22. Wells, H. G. Chloroform necrosis of the liver. *Arcb. Int. Med.*, 1: 589, 1908.

23. Howland, John and Richards, A. N. An experimental study of the metabolism and pathology of delayed chloroform poisoning. *Jour. Exper. Med.*, 11: 344, 1909.

24. Podwyssozki, W. v., Jr. Experimentelle Untersuchungen über die Regeneration der Drüsengewebe. Erster Theil. Untersuchungen über die Regeneration des Lebergewebes. *Beitr. z. patb. Anat. u. z. allg. Pbysiol.*, 1: 259–360, 1886.

25. Bizzozero, G. Ueber die Regeneration des Elemente der Gewebe unter pathologischen Bedingungen. *Centralbl. f. d. med. Wissensch.*, No. 5, 1886.

26. Ponfick, E. (Prof. in Breslau), Experimentelle Beiträge zur Pathologie der Leber. *Virchow's Archiv.*, 138: 81–117, Supplementheft, 1895.

27. von Meister, Valerian. (Aus dem Institut f. allgemeine Pathologie von Prof. W. Podwyssozki zu Kiew, Russia.) Recreation des Lebergewebes nach Abtragung ganzer Leberlappen. (Experimentelle Untersuchung.) *Beitr. z. patb. Anat. u. z. allg. Patb.*, 15: 1–116, 1894.

28. Meder, E. (Pathologischen Inst. zu Marburg.) Ueber acute Leberatrophie, mit besonderer Berücksichtigung der dabei brobachteten Regenerationerscheinungen. *Ziegler's Beitr.*, 17: 143–205, 1895.

29. Pearce, Richard M. Regenerative changes in the liver: a study of experimental lesions in the dog. *Jour. Med. Res.*, 15: 99–112, 1906.

30. Whipple, G. H. and Sperry, J. A. Chloroform poisoning, liver necrosis and repair. *Bull. Johns Hopkins Hosp.*, 20: 278, 1909.

31. Mann, Frank C. and Magath, T. B. The production of chronic liver insufficiency. *Am. Jour. Physiol.*, 59: 485, 1922.

32. Williamson, Carl S. and Mann, Frank C. Studies on the physiology of the liver: V. The hepatic factor in chloroform and phosphorus poisoning. *Am. Jour. Physiol.*, 65: 267–276, 1923.

33. Abel, J. J. and Rowntree, L. G. Phenoltetrachlorphthalein. *Jour. Pbarmacol. and Exper. Tberap.*, 1: 231, 1909.

34. Rowntree, L. G., Hurwitz, S. H. and Bloomfield, A. L. An experimental and clinical study of the value of phenoltetrachlorphthalein as a test for hepatic function. *Bull. Johns. Hopkins Hosp.*, 24: 327, 1913.

35. Whipple, G. H. and Speed, J. S. Liver function as influenced by anaesthetics and narcotics. *Jour. Exper. Med.*, 21: 203, 1915.

36. Rosenthal, Sanford M. An improved method for using phenoltetrachlorphthalein as a liver function test. *Jour. Pbarmacol. and Exper. Tberap.*, 19: 385–391, 1922.

37. Rosenthal, S. M. and White, E. C. Clinical application of bromsulphalein test for hepatic function. *J. A. M. A.*, 84: 1112, 1925.

38. Rosenthal, S. M. and Bourne, Wesley. The effect of anaesthetics on hepatic function. *J. A. M. A.*, 90: 377–379, 1928.
39. Wallace, G. B. and Diamond, J. S. Significance of urobilinogen in urine as test for liver function. *Arch. Int. Med.*, 35: 698, 1925.
40. Sheerer, E. L. Results of liver function tests. *Ann. Int. Med.*, 1: 63–67, 1927.
41. Pratt, T. W., Vanlandingham, H. W., Talley, E. E., Nelson, J. M. and Johnson, E. O. The liver function of dogs. *Amer. Jour. Physiol.*, 102: 148–152, 1932.
42. Magath, T. B. The Takata-Ara test of liver function. *Am. Jour. Digest. Dis. and Nutrition*, 2: 713–716, 1936.
43. Koehler, A. E., Brunquist, E. H. and Loevenhart, A. S. The production of acidosis by anoxaemia. *Jour. Biol. Chem.*, 64: 313, 1925.
44. Bourne, Wesley, Bruger, M. and Dreyer, N. B. The effects of sodium amytal on liver function; the rate of secretion and composition of the urine; the reaction, alkali reserve and concentration of the blood; and the body temperature. *Surg., Gynec. and Obst.*, 51: 356–360, 1930.
45. Bruger, M., Bourne, Wesley and Dreyer, N. B. Effects of avertin on liver function; the rate of secretion and composition of the urine; the reaction, alkali reserve, and concentration of the blood; and the body temperature. *Amer. Jour. Surg.*, 9: 82–87, 1930.
46. Bourne, Wesley and Raginsky, B. B. The effect of avertin upon the normal and impaired liver. *Amer. Jour. Surg.*, 14: 653–656, 1931.
47. McKim, L. H. and Bourne, Wesley. The use of avertin in multiple dressings: effects on the liver. *Can. Med. Assn. Jour.*, 28: 149–151, 1933.
48. Bourne, Wesley. Avertin anaesthesia for crippled children. *Can. Med. Assn. Jour.*, 35: 278–281, 1936.
49. Kaczander, P. Zur Frage der Lebergiftigkeit des Avertin. *Klin. Wchnschr.*, 9: 495–497, 1930.
50. Bourne, Wesley and Raginsky, B. B. Vinyl ether (vinesthine) anaesthesia in dogs: effects upon normal and impaired liver. *Brit. Jour. Anaes.*, 12: 1–8, 1935.
51. Bourne, Wesley. Divinyl oxide anaesthesia in obstetrics. *Lancet*, 1: 566 (March 17) 1934.
52. Goldschmidt, S., Ravdin, I. S. and Lucke, Baldwin. The effect of oxygen in the prevention of the liver necrosis produced by volatile anaesthetics. *Amer. Jour. Med. Sc.*, 189: 155–156, 1935.
53. Offergeld. Experimenteller Beitrag zur toxischen Wirkung des Chloroforms auf die Nieren. *Arch. f. klin. Chir.*, 75: 758–808, 1904.
54. Raginsky, B. B. and Bourne, Wesley. Effects of cyclopropane on the normal and impaired liver. *Can. Med. Assn. Jour.*, 31: 500–501, 1934.
55. Bourne, Wesley. Cyclopropane anaesthesia in obstetrics. *Lancet*, 2: 20 (July 7) 1934.
56. Roscher, F. Investigations of postoperative acidosis and ketonuria. *Acta Chir. Scand.* (74: Supp. 29: 1–238, 1933).
57. Davis, N. C. and Whipple, G. H. The influence of fasting and various diets on the liver injury effected by chloroform anaesthesia: Paper 1. *Arch. Int. Med.*, 23: 612, 1919.
58. Davis, N. C., Hall, C. C. and Whipple, G. H. The rapid construction of liver cell protein on a strict carbohydrate diet contrasted with fasting. *Arch. Int. Med.*, 23: 689, 1919.
59. Renshiro Inami. The effect of general anaesthesia upon the nitrogen metabolism, with particular reference to the time relationships. *Tôboku Jour. Exper. Med.*, 17: 39–79, 80–106, 1931.
60. Bollman, J. L. and Mann, F. C. The physiology of the liver: xxv. Allantoin and uric acid after total removal of the liver. *Amer. Jour. Physiol.*, 104: 242–246, 1933.
61. Forsgren, E. Über die Rhythmik der Leberfunktion und des inneren Stoffwechsels. *Acta Med. Scand. Suppl.*, 59: 95–96, 1934.

VENTRICULAR FIBRILLATION IN ANESTHESIA*

ARTHUR E. GUEDEL, M.D. AND PETER K. KNOEFEL, M.D.

Associate Professor of Surgery, (Anesthesia) University Southern California Medical School
LOS ANGELES, CALIF.

Assistant Professor of Pharmacology, University of Louisville School of Medicine
LOUISVILLE, KY.

CASE I. A physician administered chloroform to an eighteen year old girl in her home. As soon as anesthesia had passed through the stage of delirium into surgical anesthesia, he hurried around to the other end of the table and divulsed her spastic anal sphincter. He was probably a minute at the divulsion after which he returned to the head of the patient to find her dead. . . .

CARDIAC ventricular fibrillation is a worm-like movement of the ventricular muscle with the heart in full diastole. It consists of an unsynchronized contraction and relaxation of the individual muscle fibers, providing no circulation of blood. Its occurrence depends upon an increased activity of the sympathetic nervous system and the resultant increase of adrenin in the blood, together with a probable increase in the irritability of the ventricular muscle itself. The adrenin may be poured into the blood stream by the suprarenal glands or epinephrine may be introduced from without.

Death from ventricular fibrillation is due to cardiac anoxia. If the fibrillation passes before the reserve oxygen in the heart tissues is consumed, the heart will regain its normal activity almost immediately. If, however, the fibrillation persists until the reserve oxygen is so depleted that anoxic depression prevents the reestablishment of normal cardiac activity, the heart will fail to contract again.

Ventricular fibrillation occurs without warning. Probably it either passes in less than a minute or death results.

The approach to a surgical operation and the induction of anesthesia provide favorable circumstances for the occurrence of ventricular fibrillation. Emotional excitement, as fear, produces an increased activity of the sympathetic nervous system and consequently an increased output of adrenin from the suprarenals. This sets the stage for fibrillation in response to any added stimulus such as the delirium of the second stage of anesthesia, noises or any physical disturbance of the patient during the induction period. There is no doubt that many anesthetic deaths formerly ascribed to other causes are due to ventricular fibrillation.

The most likely place in anesthesia for the occurrence of ventricular fibrillation is in the stage of delirium, immediately after consciousness is lost. It is here that the peak of sympathetic hyperactivity is reached. It has been shown that there is an increased adrenin output from the suprarenals during anesthesia. However, this increase probably becomes less as anesthesia progresses in time or into the deeper stages.

Ventricular fibrillation is most likely to occur in the periods of life when general physiological activity is greatest, that is, between the ages of five and thirty years.

Clinical recognition of the phenomenon depends largely upon the appreciation of predisposing circumstances surrounding the case at hand. If the pulse stops without warning during the induction of anesthesia, the cause is probably ventricular fibrillation. Respiration stops almost immediately after the ventricles fibrillate. Unless the anesthetist has his finger on the pulse constantly, fibrillation will be well ad-

*The above article is excerpted from material which will shortly appear in the author's book "Inhalation Anesthesia" to be published by The Macmillan Company, through whose courtesy this publication has been made possible.

vanced before it is recognized. The respiratory cessation will likely be mistaken for one of the frequent respiratory pauses occurring at this stage of anesthesia and death occurs almost before the anesthetist is aware that anything is wrong.

If during any period of light anesthesia, when epinephrine is being used by the surgeon for hemostasis, the pulse stops without warning, there is probably a ventricular fibrillation.

Embolism, acute cardiac dilatation and apoplexy might be confused with ventricular fibrillation, although in none of these will the pulse go from normal to nothing between two heart beats.

TREATMENT

Artificial respiration with oxygen should be instituted immediately because one can never be sure at the time that circulation has ceased entirely. If the abdomen is open at the time of fibrillation, circulation may be maintained by rhythmic compression of the heart between the anterior thoracic wall and the hand, through the diaphragm. This direct cardiac massage, in the presence of adequate artificial respiration with oxygen, will prevent serious anoxemia for from half an hour to an hour, or even longer. If the fibrillation should pass during this period, it is more than likely that a normal rhythm would be reestablished. Ventricular fibrillation is preeminently the condition in which direct cardiac massage is indicated. If the condition is recognized immediately it occurs, opening the abdomen in order to prosecute this procedure is justifiable.

Ventricular fibrillation which does not pass in less than a minute is usually fatal, although the fibrillation itself may continue for many minutes beyond this period. Probably short periods of ventricular fibrillation with spontaneous recovery of normal rhythm have occurred many times without being recognized.

In the light of the foregoing it would seem that there is nothing to be done about ventricular fibrillation, once it is started, but to maintain artificial circulation by direct cardiac massage, in the presence of artificial respiration with pure oxygen, in the hope that the fibrillation might pass of its own accord.

PREVENTION

This lies in holding down the activity of the sympathetic nervous system and thus the output of adrenin from the suprarenals, and the avoidance of any external stimuli during the induction of anesthesia.

Any preanesthetic medication which will prevent sympathetic hyperactivity is of value. Morphine fails to do this. Deaths have occurred from ventricular fibrillation in individuals who had received the usual preanesthetic dose of morphine.

The barbituric acid derivatives are effective depressants of the sympathetic nervous system. They render the production of fibrillation in animals more difficult and are no doubt of the same value in man. The degree of protection afforded by these drugs is in proportion to the dose administered.

Atropine and scopolamine are of value in that they prevent reflexly excited activity of the cardiac vagus from deranging the normal gradient of cardiac excitability.

Too much emphasis cannot be placed upon the necessity of avoiding any disturbance of the patient during induction. Such things as beginning the preparation of the operative field, or the surgical procedure itself, before anesthesia is complete, are dangerous. Knowing the danger zone to be the second stage of anesthesia, we must carry anesthesia through this stage as rapidly as possible.

The use of epinephrine in amounts sufficient to control bleeding during general anesthesia is to be condemned. When epinephrine must be used in the surgical procedure it should be used sparingly. Deeper anesthesia is here indicated in order to reduce activity of the sympathetic nervous system. But even in deep surgical anesthesia it is possible to introduce enough

epinephrine into the blood stream to produce ventricular fibrillation.

Levy showed, and it has since been noted by others, that ventricular fibrillation is produced much more easily under anesthesia with chloroform, than with other anesthetic agents. Published discussions of the relationship between chloroform and ventricular fibrillation have been such as seemingly to absolve the other anesthetic agents from participation in the production of the phenomenon. The other agents cannot be absolved from blame. Although chloroform is the greatest offender, ventricular fibrillation must be considered a potential danger in every anesthesia, no matter what agent is used.

Aside from placing chloroform first and ethyl chloride possibly second, we cannot classify the other anesthetic drugs with relation to the frequency of occurrence of this phenomenon.

ILLUSTRATIVE CASES

Case II. (Year 1931.) Donald, the seven year old son of a prominent physician, was having an emergency myringotomy; and Donald was full of fear. About his couch were his father, a neighbor, the myringotomist and the anesthetist. The myringotomist, with his lancet poised, gave the signal and the anesthetist went to work. Donald struggled. The stream of ethyl chloride was too small and the anesthetic induction progressed too slowly. A full minute was consumed at induction, at the end of which time the neighbor was sweating, the myringotomist was shifting from foot to foot and the father was maintaining an enforced calm dignity but with an anxious look in his eye. The embarrassed anesthetist gave way to the feelings of the gallery and as soon as Donald ceased struggling, said "Go ahead." It was too soon. With the ear drum incised, the anesthetist stood up and, heaving a sigh of relief, said "I'm glad that's over." Then he looked at the boy. The boy looked dead.

Respiration? None. Color? Flat gray with mottled cyanosis. The anesthetist quickly listened with ear to chest. There were no heart sounds. The patient was jerked up by the feet and while hanging thus, his precordium was vigorously pounded for perhaps fifteen seconds. Then he breathed. Another application of ear to chest revealed rapid though normal heart sounds. Not more than thirty seconds had elapsed since the myringotomy. In a minute more he was awake and crying.

Discussion. The anesthetist was to blame for permitting the painful operation before the child was sufficiently anesthetised. The clumsy induction with the fearful struggling had set the stage well for ventricular fibrillation, with sympathetic activity at its peak and blood adrenin high. The incision provided the required added stimulus to produce the fibrillation. The fibrillation passed before anoxic depression rendered the heart unresponsive to its normal stimulus. It is doubtful whether or not the violent resuscitative measures influenced the outcome. Probably the fibrillation passed in spite of the traumatic stimulation.

Case III. (Year 1936.) A thirty-three year old devout Catholic was brought to the operating room of a Protestant hospital at nine o'clock one morning for the surgical abortion of a two month's pregnancy. Two previous classical cesarean sections, two living children, and the physician's fear of uterine rupture in the next labor were reasons for the abortion.

She entered the hospital at seven thirty o'clock and received morphine gr. $\frac{1}{4}$ with atropine gr. $\frac{1}{150}$ at eight o'clock. The surgeon, her close friend, chatted with her reassuringly for a moment as she lay on the operating table. Her attitude was almost too calm.

After about fifteen seconds of cyclopropane (four or five breaths) she uttered a muffled scream, thrust her arms into the air, became rigid for possibly three seconds, then relaxed and took one deep inspiration. Guessing "ventricular fibrillation," the anesthetist quickly sought the carotid pulse. It was not there. Ear to precordium revealed no heart sounds. Vigorous precordial massage, with artificial respiration of oxygen was instituted at once. These and all other resuscitative measures failed.

Discussion. What was the psychic state of this woman with reference to the proposed operation? Her calm self control

was that of a dominant will. It was later learned that she was like that. But will power cannot control sympathetic activity and her fibrillation stage was set, without doubt, before the anesthesia was started. An emotional upheaval as anesthesia reached the delirium stage, set off the mechanism.

Case IV. (Year 1921.) A thirty year old virile business man was to have a tonsillectomy and a resection of the nasal septum under general anesthesia. The preanesthetic medication was morphine gr. ¼ with atropine gr. 1/150. To control the bleeding during the septum operation, the nares were packed with gauze saturated with 1–1000 "adrenaline" before the drop ether anesthesia was started. Four or five minutes after the induction was begun, at about the time of the second stage of anesthesia, he suddenly became restless, took two or three deep breaths and died.

Discussion. Hyperactivity of the sympathetic nervous system with its resultant outpouring of adrenin from the suprarenals, plus the "adrenalin" absorbed from the nasal pack, prepared the way for this fibrillation. The mechanism which provoked the fibrillation could have been a terrorizing dream as the delirium stage of anesthesia was reached, or it could have been simply the combination of peak activity of the sympathetic nervous system together with an overload of epinephrine in the blood.

Necropsy showed no cause for death.

Case V. (Year 1921.) A thirty-two year old woman was having a frontal sinus operation under ether anesthesia. With the anterior sinus wall removed, the bleeding was obscuring the field, and the surgeon was sloshing 1–1000 "adrenalin" into the sinus to control the bleeding. It was fairly effective but a lot of sloshing was required. About half an ounce of "adrenalin" was used before the patient suddenly died. Necropsy disclosed no cause for death.

Discussion. There could have been no provocative stimulus here. It was just a case of too much epinephrine with possibly a lightening of the anesthesia at the time of fibrillation.

Case VI. (Year about 1908.) This was in the day when deaths under chloroform anesthesia were attributed to a direct toxic depression of the heart by the chloroform. The patient, a sturdy young mechanic, had received strychnine sulfate gr. 1/30 prior to the anesthesia to support the heart against the chloroform. The operation was the breaking down of a fibrous ankylosis of the knee joint. After administering chloroform to light anesthesia, the physician hurried around to the side of the table and broke down the ankylosis. Not more than a minute was consumed in the operation but the patient was dead when it was finished.

Discussion. In this case as well as in the case cited in the opening paragraph of this article, the answer is a combination of sympathetic hyperactivity, high adrenin in the blood and a heightened irritability of the ventricular muscle itself by the chloroform, plus the heavy traumatism under an insufficiently deep anesthesia. There was no necropsy in either case.

APPLIED PHARMACOLOGY OF LOCAL ANESTHETICS*

RAYMOND N. BIETER, M.D., PH.D.

Associate Professor of Pharmacology, University of Minnesota Medical School

MINNEAPOLIS, MINN.

THE great advances in surgery of the past fifty years have been due to a remarkable cooperation obtained from a variety of separate fields of research. Next to aseptic and antiseptic surgical technique, perhaps no single field of therapeutics has contributed more to the comfort of the patient undergoing surgery than has local anesthesia. In 1880, the pharmacologist, von Anrep,[2] discovered the local anesthetic properties of cocaine HCl when its aqueous solutions were injected subcutaneously and therefore recommended its use for this purpose. However, it was not until after Koller[26] reported his experimental and clinical results in surgery of the eye, in 1884, that local anesthesia came into clinical use. In contrast to its modest beginnings, and to appreciate its common use today, one has only to look at the statistical reports of a surgical institute such as the Mayo Clinic,[30] to note that local anesthesia is employed, wholly or in part, in over 50 per cent of patients to whom anesthetic agents are administered.

The reasons for this growth in use are several. Perhaps, first of all, comes ease of administration as compared with inhalation anesthesia. Again for surgery of a part of the body, a local anesthesia is to be preferred to a complete whole anesthesia of the body. There is the unpleasant element with general anesthetics of bodily injury, such as disturbances of acid base balance, and possible injury to important organs such as the liver, heart and kidneys. These, as a rule, are minimized by local anesthesia. There is the element of shock; an unsatisfactory general anesthesia may be much more dangerous from this standpoint than a local anesthesia.

LOCAL ANESTHETIC ACTION

The local anesthetics in common use today are all alkaloids. Most of them are synthetic preparations. The alkaloidal bases are all highly lipoid soluble, which means that they can be taken up by lipoid nerve structures. They can all be prepared as water soluble salts. The aqueous solutions for clinical use must be non-irritant. When a solution of suitable concentration of a local anesthetic is applied or injected into a living body there occurs what appears to be a local selective action on any part of a nerve fiber or even a nerve cell. This is the basis for the local anesthetic action. Certain chemical and physicochemical properties of local anesthetics, many of which have been described and studied, play a role in the development of this action. One of the most important factors is probably associated with the hydrolysis of local anesthetic salts in solution produced by even small amounts of alkali, as are present in most tissue fluids. This hydrolysis liberates the alkaloidal base which can then be taken up more readily by the nerve structures. That the presence of acid seems to inhibit local anesthesia is shown by the fact that it is difficult to anesthetize acute abscesses, and by the fact, according to Gerlough,[17] that a 0.25 per cent butyn solution at a *p*H of 5.5 to 6 produces very little anesthesia of the rabbits' cornea. The same concentration of butyn at a *p*H of 7.4, however, produces a very considerable duration of anesthesia. The decreased hydrolysis produced by acid could easily explain these anesthetic changes. Another important

* From the Department of Pharmacology, The University of Minnesota Medical School, Minneapolis, Minn.

factor in the production of local anesthesia is undoubtedly ionization of the alkaloidal salt which produces an ion of the anesthetic base carrying a + electric charge. A nerve structure carrying a − electric charge should then readily take up this ion.

The local anesthetic action produced by the drugs of this series is a complete depression of the function of a nerve structure. It occurs without a previous stimulation, and it later subsides and the function of the nerve returns again to normal. The selective action of the local anesthetics on nervous tissue is not a uniform depression, however. This has been demonstrated on the isolated saphenous nerve of the cat by Heinbecker, Bishop and O'Leary.[21] In their experiments, the first action potential to disappear was that from unmyelinated fibers; the second, the potential from the smallest thinly myelinated fibers; the third, the potential from smaller relatively thinly myelinated fibers, and so on until the last potential to disappear came from the large thickly myelinated fibers. The corresponding loss of sensations observed by them was, first vasoconstriction, second temperature, third pain, fourth touch, and lastly joint and pressure sense. Obviously, a satisfactory local anesthesia must include at least the first three groups of fibers in order to eliminate pain.

Further evidence of the selective action of local anesthetics can be obtained from the application of solutions to an isolated mixed nerve such as the sciatic. In frogs, Alms[1] showed many years ago that cocaine solutions produce a sensory anesthesia without paralysis of the motor fibers. It is commonly known today, however, that paralysis of motor fibers can be produced with sufficiently high concentrations, but that the depressant action on motor fibers is more difficult to obtain than the depressant or anesthetic action on sensory fibers. Gasser and Erlanger[16] have shown that in the mixed nerves of frogs and dogs, cocaine produces a sensory anesthesia before motor paralysis. This differentiation they ascribe to the fact that the sensory nerve fibers, as a rule, are smaller in diameter than motor nerve fibers.

To determine the efficiency of local anesthetics many methods for studying their comparative actions have been described. These are reviewed in most textbooks, by Munch[35] and also by Hirschfelder and Bieter.[23] To obtain comparative results most applicable to infiltration anesthesia, the best method of study is perhaps the method of producing intracutaneous wheal anesthesia in the human skin. This was introduced by Braun[7] and has been extensively employed by many investigators and especially by Sollmann.[41] A small volume of the anesthetic solution, usually less than 0.5 c.c., is injected into the skin on the flexor surface of the human forearm. The minimal anesthetic concentration and the duration of anesthesia can be determined with about as much accuracy as with other methods of testing anesthetics. Table 1, taken from Sollmann, gives the duration of anesthesia produced by this method with a series of concentrations of procaine and cocaine, beginning with the minimal anesthetic concentration. Solutions containing 1 per cent or less of these drugs alone produce a very short anesthesia, almost too short for most surgical purposes.

One of the chief special applications of local anesthesia which is of great interest and usefulness to anesthetists and surgeons is spinal anesthesia. This term was first used by Corning[8] in 1885, but it was not until after Bier[4] in 1899, first injected cocaine intraspinally in man that its clinical use began. Since that time spinal anesthesia has undergone waves of popularity with each new introduction of a local anesthetic. Within recent years much valuable information on this form of anesthesia has been obtained. The selective action of local anesthetics administered intraspinally is again apparent but in a slightly different manner than outside the spinal canal. Heinbecker, Bishop and O'Leary[21] in surgical patients have shown that the changes in sensations are as follows: (1) there occurs an increase in skin temperature, probably

associated with a paralytic effect on sympathetic vasoconstrictor fibers, (2) there is a loss of temperature and pain, (3) after a short interval motor paralysis occurs, and finally (4) there occurs a loss of joint, pressure and touch sensations. Emmett[14] has also reported that anesthesia to pain occurs before motor paralysis and disappears last. On the other hand, Bieter, Cunningham, Lenz and McNearney[5] found that in the rabbit, motor paralysis occurs before sensory anesthesia and is the last to disappear and, furthermore, that the minimal anesthetic concentration is lower for motor paralysis than for sensory anesthesia. This profound motor effect in spinal anesthesia is well known. The relaxation this affords, especially for surgery of the pelvis and lower abdomen is one of the chief advantages of this form of anesthesia. Why the intraspinal injection of local anesthetics should produce such a marked motor paralysis as compared with their use outside of the subarachnoidal space is not known, unless it is due to the fact that extraspinally the nerves are surrounded by protective sheaths whereas intraspinally the nerve structures lie more or less bare.

TABLE I
DURATION OT SENSORY ANESTHESIA IN WHEALS
(Compiled by Sollmann[41])

Per Cent Solution	Cocaine, Minutes	Procaine, Minutes
0.031	5.0	2.0– 8.5
0.062	5.0– 7.0	6.5
0.125	6.0–15.0	0.5–10.0
0.25	8.0–14.0	5.0–10.0
0.5	10.0–18.0	9.0–14.0
1.0	20.0–25.0	12.0–17.0
5.0	34.0–54.0	17.0–39.0
10.0	.....	27.0

Data on the duration of spinal anesthetics is almost completely lacking in the literature. Yet from the standpoint of the patient this must be one of the chief requirements of an anesthetic. Recently Bieter, McNearney, Cunningham and Lenz[6] have reported on the duration of anesthesia produced by the intraspinal injection of six local anesthetics in the rabbit. They have found, as is the case elsewhere, that the duration increases with increasing concentrations of the local anesthetics. This is confirmation of the opinion of Lundy.[31] Table II shows the average duration of anesthesia produced by six concentrations of procaine HCl, as obtained by them. The first concentration is the minimal anesthetic dose and the last, the minimal lethal dose. By comparison with Table I it can be seen that the increase in duration of anesthesia, intraspinally, is more proportional to the concentration than it is in the human skin. They suggested that this may indicate that systemic absorption from within the subarachnoidal space, at least in the rabbit, is slower than from within the human skin. Of the other five local anesthetics studied by these investigators, tutocaine, panthesine and metycaine offer no advantage over procaine HCl as regards duration of anesthesia. On the other hand, both pontocaine and nupercaine can produce an anesthesia lasting from three to four times that of procaine HCl.

PROLONGATION OF LOCAL ANESTHETIC ACTION

Next to the introduction of the local anesthetics themselves, the greatest advance in this field was made when Braun[7] in 1903 demonstrated that minute quantities of epinephrine added to local anesthetic solutions greatly prolonged the duration of anesthesia for infiltration and

TABLE II
SPINAL ANESTHESIA IN THE RABBIT WITH PROCAINE HCL[6]

Per Cent Solution	Average Duration of Sensory Anesthesia, Minutes
0.9 (M.A.D.*)	16.0
1.25	28.0
2.5	45.0
4.0	59.0
5.0	72.0
6.0 (M.L.D.†)	105.0

* Minimal anesthetic dose.
† Minimal lethal dose.

block injections. This was later confirmed by Sollmann[41] who showed that for cocaine there was actually a potentiation, but for most of the remaining drugs he studied it was a simple prolongation. This beneficial lengthening of the anesthesia is very striking with procaine. Epinephrine also produces a prolongation of anesthesia with the more recently introduced local anesthetics. This action is due to a local vasoconstriction produced by the epinephrine which greatly decreases the blood flow, thereby slowing the absorption. As a result, much smaller concentrations of the local anesthetics may be used, the resulting anesthesia is still greatly prolonged, and the danger of toxic symptoms occurring is greatly reduced. The concentration of epinephrine ordinarily added to local anesthetic solutions for this purpose ranges from 1 part in 50,000 to 1 part in 200,000 or even less. Experimental data obtained from the literature on the duration of anesthesia thus produced is summarized by Hirschfelder and Bieter.[23]

TABLE III

EFFECT OF EPINEPHRINE ON DURATION OF HUMAN WHEAL ANESTHESIA

Drug, 0.125 Per Cent Solutions	Epinephrine Content				
	0, Minutes	1:500,000, Minutes	1:200,000, Minutes	1:100,000, Minutes	1:50,000, Minutes
Procaine HCl	16.6	65.4	89.2	87.2	83.0
Metycaine	18.5	54.8	68.5	59.5	71.9
Cocaine HCl	20.3	59.9	88.2	85.3	88.1
Panthesine	20.6	84.2	125.1	111.8	94.2

For a number of years the author has been collecting data on this subject in class experiments on medical and dental students in the Laboratory of the Department of Pharmacology. Table III shows the average duration of anesthesia produced by four local anesthetics, without added epinephrine and with four concentrations of epinephrine. The data has been obtained from more than 750 individuals. The injections were made on the flexor side of the forearm. The dosage per injection was 0.2 c.c. The epinephrine resulted in a prolongation of anesthesia of each drug three or more times. The least prolongation occurred with metycaine; a greater and almost equal prolongation occurred with procaine and cocaine; and the greatest effect occurred with panthesine. It is rather interesting to note that a uniform increase in duration, proportional to the epinephrine content, did not occur. The explanation of this variation may be, in part, that the more concentrated epinephrine solutions tend to produce a local acidosis which hinders the continuance of the anesthesia.[37] These results will be reported in detail elsewhere.

Recently a new vasoconstrictor substance has been prepared synthetically and introduced for use with local anesthetic solutions. It is 3,4-dihydroxy-phenyl-propanol-amine-HCl and is commonly called cobefrin hydrochloride. This drug, according to Tainter,[44] has $\frac{1}{12}$ the degree of pressor activity of epinephrine, and, in white rats, $\frac{1}{53}$ the toxicity of epinephrine. It has been shown to prolong the local anesthetic action of procaine. A few intracutaneous wheal experiments with this drug have been conducted by the author using a concentration of cobefrin five times that used with epinephrine. From 6 to 10 experiments were conducted with each concentration. These results are shown in Table IV. As a general rule these concentrations of cobefrin did not give as great

a prolongation of anesthesia as the corresponding ⅕ concentrations of epinephrine. Further experimental work on this substance is being conducted.

Many other substances have been shown to potentiate the action of local anesthetics. Gros[18] first showed that sodium bicarbonate added to local anesthetic solutions shortened the incidence of anesthesia for isolated nerve trunks. Later Sollmann[42] showed that this salt increased the efficiency of cocaine and procaine eight times for motor fibers, and from two to four times for sensory fibers, in an isolated nerve. This action is due to a liberation of the anesthetic base by the sodium bicarbonate which will then penetrate the nerve trunk more readily. Sollmann[41] has also shown that this salt does not improve the efficiency of intracutaneous anesthesia and this probably holds for infiltration anesthesia as well. However, as Sollmann[43] remarks, the addition of not more than 0.5 per cent sodium bicarbonate to local anesthetic solutions may be of value for block and spinal anesthesia. Recently Gwinn and Ferber[19] reported that sodium bicarbonate added to procaine solutions for mandibular block shortened both the incidence and duration of the anesthesia in human patients, consequently little improvement was obtained.

Table IV
EFFECT OF COBEFRIN ON DURATION OF HUMAN WHEAL ANESTHESIA

Drug, 0.125 Per Cent Solutions	Cobefrin Content			
	1:100,000, Minutes	1:40,000, Minutes	1:20,000, Minutes	1:10,000, Minutes
Procaine HCl..	67	70	66	82
Metycaine.....	..	75	65	67
Cocaine HCl...	..	75	60	67
Panthesine.....	..	105	136	71

Finally it should be noted that there is a complete lack of proved, safe potentiating substances for use in spinal anesthesia. In this respect this latter field is still in an unsatisfactory stage comparable to ordinary local anesthesia without epinephrine and cobefrin.

TOXICITY

Next to the production of a suitable nonirritant anesthesia, the most important property of a local anesthetic is its toxicity. Despite the fact that data is available on the toxicity in animals of all of the local anesthetics in common use, untoward reactions have occurred altogether too commonly. This is the opinion of the author based upon the reports of Mayer,[34] of the Local Anesthetic Committee of the American Medical Association, and upon the reports of the new local anesthetic introductions of recent years. It, therefore, is evident that there are no uniform rules easily available for determination of clinical dosage. The minimal lethal doses determined on animals are not the minimal lethal doses for patients. A very considerable reduction below these minimal lethal doses for clinical use is absolutely essential, because sick human beings are undoubtedly much more sensitive to the systemic effects of local anesthetics than are healthy normals.

The Local Anesthetic Committee of the American Medical Association[34] has made several recommendations as regards safe doses of local anesthetics. Two of their recommended safe doses are: cocaine, 1 to 1.5 grains and butyn 1 grain. In studying a summary of the available literature on lethal doses of the local anesthetics in animals (Hirschfelder and Bieter[23]), it appeared to the author that these total safe doses for patients were quite like the minimal lethal doses per kilogram of guinea-pig administered by subcutaneous injection. It is the opinion of the author, therefore, in the complete absence of any definite criteria for determining safe human dosages, that these minimal lethal doses from the guinea-pig be considered as *total safe human doses* in a manner similar to that recommended by Mayer.[34] Table v shows this data for eleven local anesthetics.

The table includes the range of lethal doses given in the compilation mentioned, as well as the average figure for each minimal lethal dose in the guinea-pig, from this compilation, as the *total safe human dose*, in milligrams and in grains, to be administered at any one time. It is to be noted that the total safe dose of procaine, in this table, is in agreement with that given by Hertzler.[22] Certain discrepancies become apparent immediately. The safe dose of procaine for spinal anesthesia should be much smaller. The same should be true for injection of procaine into highly vascular areas. *Therefore for spinal anesthesia and for injection into highly vascular areas these safe doses should be cut in half.* This reduction of the safe dose of procaine for spinal anesthesia is in agreement with the maximal safe dose of 200 milligrams of this drug employed by Lundy.[32] It should be added that this table is to be considered as a stepping stone to something better.

Table V

TABLE OF PROPOSED TOTAL SAFE HUMAN DOSES
Prepared from compilation of minimal lethal doses, subcutaneous injections to guinea-pigs, by Hirschfelder and Bieter[23]

Drug	Range of Minimal Lethal Doses in Mgm. per Kg. of Guinea-pig, Subcutaneous Injection	Average Total Safe Dose Excluding Injections Intraspinally and into Highly Vascular Tissue	
		Mgm.	Grains
Procaine HCl	350–600	430	6–7
Larocaine	200	200	3
Tutocaine	116–270	193	3
Panthesine	75–150	112	2
Metycaine	Not determined	100*	1.5
Alypine	60–100	72	1
Butyn	70	70	1
Phenacaine HCl	50– 60	53	1
Cocaine HCl	20– 80	50	1
Pontocaine	Not determined	20*	⅓
Nupercaine	7.5– 15	11	⅙

* Determined by comparison with data in other species of animals.

That the toxicity of local anesthetics varies greatly, depending upon the method of application, is quite evident. Consider procaine for example. A few average subcutaneous minimal lethal doses per kilogram of body weight are: for the guinea-pig 430 mgm., rabbit 460 mgm., and cat 450 mgm. By means of intravenous injections the minimal lethal doses become 50 mgm., 55 mgm., and 45 mgm., for these species respectively. Similar differences are to be noted with other local anesthetics. Greater care should therefore be utilized when the local anesthetics are applied to highly vascular areas such as the nose, throat and urethra, than, for example, the abdominal wall. This is also evident from the report of Mayer,[34] which included more deaths following the application of local anesthetics to the throat and urethra than to other parts of the body.

The systemic toxic effects of local anesthetics appear to be due primarily to three main actions, the most important being on the respiratory center. Relatively small doses of most of the local anesthetics entering the blood stream cause a stimulation of this center, whereas larger doses cause a depression which ultimately becomes a paralysis. This is perhaps the chief cause of death. This action, experimentally, is most commonly produced by procaine, cocaine, metycaine, panthesine, tutocaine, butyn and perhaps pontocaine. A second action is on the circulation where again there may first appear a simulation with a rise of blood pressure, followed by a depression with a marked fall of blood pressure. The most toxic for this system, appears to be nupercaine which, according to Lipschitz and Laubender,[29] most commonly produces death by cardiac depression, in rabbits. The third action appears to be due to an action on the cerebrospinal system. It is manifest by the production of convulsions, which may later give way to marked depression and death probably from exhaustion. All of the local anesthetics can produce this effect.

At the present time many of these reactions can be prevented. The addition of epinephrine to local anesthetic solutions for infiltration and nerve block is one of

the most important factors to decrease or slow absorption. This one improvement in local anesthesia has perhaps done more to render local anesthesia prolonged and safe than any other factor, except the substitution of the relatively less toxic procaine for the other members of the group for injection anesthesia. The use of epinephrine, however, is not entirely free of danger. Serafin[40] has reported that a concentration of 1:20,000 epinephrine in 2 per cent procaine HCl solution may produce local death of tissue. It is the opinion of Sollmann[43] that for most surgical purposes the maximum concentration should not exceed 1:50,000. The total dose of epinephrine injected should be no more than one milligram (Mayer[34]). A larger dose, especially in excitable or susceptible patients, may produce the minor toxic symptoms of the drug such as anxiety, tremors, nervousness, palpitation, etc. Due to the synergism between epinephrine and the local anesthetics, especially cocaine, these symptoms may therefore become more severe.

In place of epinephrine the new vasoconstrictor, cobefrin, may be added to local anesthetic solutions for injection. This drug also delays absorption and therefore should also reduce possible toxic reactions. The maximum concentration that is safe to use has, as yet, not been determined. The recommended concentrations for preliminary study are about five times that of epinephrine. Because Tainter[44] has shown that it is much less toxic than epinephrine, it may, in the above concentrations, be less dangerous than epinephrine. Furthermore, Winter[47] cites some experimental evidence to indicate that novocaine plus epinephrine, intravenously in rats, is more toxic than the same concentration of novocaine plus five times the concentration of cobefrin. Additional pharmacological work and further confirmation is much to be desired.

Another important procedure in the prevention of toxic reactions is the preliminary administration of a member of the barbituric acid group of hypnotics. Other hypnotics had been shown previously to confer some protection to animals. The importance of this action, however, was not properly emphasized, until Tatum, Atkinson and Collins[45,46] demonstrated that a member of the barbital group could actually raise the lethal dose of cocaine in animals. This protection increased with increasing brain development so was therefore greatest in monkeys. Later, Knoefel, Herwick and Loevenhart[25] confirmed these observations and showed that sodium amytal conferred a greater degree of protection than either sodium barbital or sodium phenobarbital. These findings have been repeatedly confirmed by reports of the clinical use of the barbital hypnotics preliminary to the administration of local anesthetics. These hypnotic drugs have greatly reduced the incidence of toxic symptoms.

The destruction and elimination of local anesthetics occurs chiefly in the liver and kidneys. It was shown by Hatcher and Eggleston[20] that a fatal dose of procaine for a cat was destroyed in about twenty minutes by the animal's liver. With cocaine the destruction required from three to four times as long a time interval. This problem has recently been reinvestigated by Dunlap[13] in the dog. In this animal the liver also produced the most rapid detoxification of procaine, although he obtained evidence that other tissues can do likewise at a much slower rate. He found further that complete destruction required about one hour. MacDonald and Israels,[33] working on cats, found about the same time to be necessary, and also recorded the marked slowness with which cocaine was destroyed and eliminated by the cat's body. From the available data, it appears that the other local anesthetics are destroyed and eliminated somewhat slower than procaine, but faster than cocaine. The use of local anesthetics in patients with liver disease is therefore not without danger.

The toxic symptoms of intraspinally injected local anesthetics are somewhat different from those produced by other

methods of administration, and therefore merit special consideration. Our knowledge of the factors involved is due chiefly to the work of Ferguson and North,[15] Co Tui and Standard,[12] Seevers and Waters,[39] and Johnston and Henderson.[24] Following the lumbar injection of a local anesthetic, some of the spinal fluid containing the local anesthetic rises to the thoracic region and occasionally to the cervical region. Coincident with this rise of the anesthetic there occurs an increasing reduction of respiratory excursions and a sharp drop in blood pressure. The decreased respiratory excursions are due to an ascending paralysis of the intercostal nerve structures within the subarachnoidal space. The drop in blood pressure is probably due to a number of factors, such as a paralysis, within the subarachnoidal space, of the rami communicantes to the sympathetic chains; a paralysis, in the cervical portion of the subarachnoidal space, of cardiac accelerator fibers; an interference with oxygenation of the whole body due to the lessened respiratory activity; and a local decrease in circulation due to the marked relaxation of muscles produced in the lower half to two-thirds of the body.

The occurrence of other toxic manifestations in man have been collected and reported by Koster and Weintrob.[27] Similar symptoms have been reported as occurring in the dog by other investigators. In the rabbit, Bieter, Cunningham, Lenz and McNearney[5] have reported that lethal concentrations of the six local anesthetics studied by them commonly produce permanent paralyses of the muscles of the lower extremities. In addition they observed other irritative or toxic symptoms such as ocular complications, convulsions and spasticities of the head, neck and forelegs. This last named group of complications occurred most commonly with pontocaine and nupercaine, to a lesser extent with metycaine, panthesine and tutocaine, but never with procaine.

The common cause of death in spinal anesthesia has been ascribed by Johnston and Henderson[24] to paralysis of the intercostal nerve structures in the thoracic region, followed by phrenic root paralysis in the cervical region. On the other hand Co Tui[11] cites evidence to indicate that phrenic nerve paralysis is of central origin. In rabbits, Bieter, Cunningham, Lenz and McNearney[5] observed as the most common type of death, an ascending paralysis of the intercostals followed by a sudden cessation of diaphragmatic respiration. In a much smaller group of rabbits they observed further that intercostal and diaphragmatic respiratory movements stopped simultaneously. They are of the opinion that the latter type of death was due to a central paralytic effect, in a manner similar to that occurring in dogs following the intracisternal injections of procaine, as reported by Co Tui and Standard.[12] Further evidence to indicate that paralysis of the respiratory mechanisms is the chief cause of death in spinal anesthesia can be obtained from the data of Bieter et al.[5] on the duration of the heart beat after cessation of respiration. In all of their animals, after respiratory paralysis the hearts continued to beat regularly, on an average of three to ten minutes following the injections of procaine, tutocaine, panthesine, metycaine and pontocaine. Following respiratory paralysis produced by nupercaine, however, the hearts were never observed to beat regularly. Only a few irregular and weak contractions were observed.

Bieter, Cunningham, Lenz and McNearney[5] have also determined the intraspinal minimal lethal doses of the six local anesthetics studied in rabbits. This dosage for procaine averaged 18.3 mgm. per kilogram of body weight in a 6 per cent solution. Compared to the average minimal lethal dose by intravenous injection which is 55 mgm. per kilogram, this is a rather marked increase in toxicity. In the dog, Co Tui[11] found the lethal dose to be about 45 mgm. per kilogram. No data is available for comparison with intravenous lethal doses. However, it is interesting to note that procaine intraspinally in the dog is

less toxic than in the rabbit. This might indicate that the presence of spinal fluid, as in the dog, has an inhibiting action on the toxic effects of this local anesthetic compared to conditions in the rabbit where no profuse amount of spinal fluid is present. If this is true, similar differences, compared to the rabbit, should exist in man.

The prevention and control of the toxic reactions produced by spinal anesthetics has again lagged behind that in other forms of local anesthesia. One of the most beneficial preventive measures is the administration of ephedrine sulphate preliminary to the spinal injection, as was introduced by Ockerblad and Dillon,[36] and Rudolph and Graham.[38] This drug has a prolonged vasoconstrictor action and can materially control the great drop in blood pressure that tends to occur in spinal anesthesia. It appears to be more efficacious as a preventive measure than as a therapeutic measure once the blood pressure has fallen. For the prevention of the respiratory depression no drug is of great value. With a severe decrease in respiratory excursions the administration of oxygen and carbon dioxide is undoubtedly of value. In the presence of completely flaccid respiratory muscles, however, the last resort, as Babcock[3] states, is mouth to mouth insufflation. What is needed is a new local anesthetic with relatively less depressant action on motor nerve structures so that anesthesia of the respiratory motor nerves will not occur.

Because of the protection afforded by barbital hypnotics to the toxic actions of local anesthetics administered extraspinally, these drugs are being used preliminary to spinal anesthesia. Their use is questionable, however, because Co Tui[10] has shown that sodium amytal increases the toxicity of procaine administered intracisternally in the dog. On the other hand, morphine and morphine-scopolamine in small but effective doses do not do so. This subject requires further study, especially with the newer short acting members of the barbital group.

The Trendelenburg position has been strongly recommended in spinal anesthesia to increase the blood flow to the head and vital centers. In dogs, Co Tui[11] has again shown that with the head down 17°, the lethal dose is decreased almost 50 per cent. Any appreciable amount of this position should therefore be dangerous, especially because, as Co Tui[9,11] has shown, the lethal dose of procaine in dogs given by intracisternal injection is much smaller than the lethal dose administered by lumbar injection. Recently, Koster, Shapiro, and Leikensohn[28] have shown in patients that, following the lumbar injection of 150 mgm. of procaine HCl in about a 4 per cent solution, the patient's spinal fluid contains from 6 to 1 mgm. of procaine HCl per cubic centimeter for as long as thirty minutes after the injection. It would seem therefore that a Trendelenburg position of more than a few degrees would be extremely dangerous immediately after the injection. Because the concentration of procaine in the spinal fluid falls rapidly, the danger would be much decreased at about thirty minutes.

CLINICAL APPLICATIONS

The safest local anesthetic for all injection forms of local anesthesia is procaine HCl. The duration of its anesthesia is fairly satisfactory, though not sufficient for all purposes.

For infiltration anesthesia, it should be used in the lowest possible concentrations. The strongest solutions for this purpose should be 0.5 per cent, but where possible 0.25 per cent solutions should be used. Even 0.125 per cent concentrations, experimentally, produce a satisfactory anesthesia; consequently this solution should be usable at least in some forms of anesthesia. Epinephrine or cobefrin should be added to the solutions for injection purposes, except in spinal anesthesia. In certain regions where a vasoconstrictor may be contraindicated, as in the fingers and toes, a tourniquet should be applied.

For block anesthesia procaine HCl should be used in the lowest possible concentrations. Two per cent solutions should be the average maximum, yet it appears that for most purposes a 1 per cent solution should suffice.

For spinal anesthesia procaine HCl is again the drug of choice. Its maximum dosage should be 200 mgm. and the maximum concentration to inject into the subarachnoidal space should be 4 to 5 per cent.

The other local anesthetics should be used as substitutes for procaine HCl only when there is a contraindication for this drug, such as hypersensitivity or failure in the anesthetic action. They should be used cautiously. The concentration to be used should be as much smaller than that of procaine HCl as the drug is more toxic. Thus for a drug that is twice as toxic as procaine HCl, its comparable concentration should be one-half that of procaine HCl. If these concentrations of the substitutes fail to give a satisfactory anesthesia, at least until great experience has been obtained in local anesthesia, this form of anesthesia should be discarded in favor of some other form.

Where possible, measures for prevention of toxic reactions should always be used. Furthermore, anesthetists and surgeons should constantly be prepared to treat toxic reactions if they occur.

SUMMARY

The intelligent and safe use of local anesthetics requires a thorough knowledge of their pharmacological actions, the potentiation of these actions, their toxicity, and the prevention and control of toxic reactions, by anesthetists and surgeons.

This involves more than a superficial knowledge of these drugs.

REFERENCES

1. Alms, H. Die Wirkung des Cocains auf die peripherischen Nerven. *Arcb. Anat. u. Physiol.* (Physiol. Abt., Supplement-Band), 1886, p. 293.
2. Anrep, B. von. Ueber die physiologische Wirkung des Cocain. *Arcb. f. d. ges. Physiol.*, 21: 38, 1880.
3. Babcock, W. W. Spinal anesthesia. *Am. Jour. Surg.*, 5: 571, 1928.
4. Bier, A. Versuche über Cocainisirung des Rückenmarkes. *Deutscb. Zeitscbr. f. Cbir.*, 51: 361, 1899.
5. Bieter, R. N., Cunningham, R. W., Lenz, Oa and McNearney, J. J. Threshold anesthetic and lethal concentrations of certain spinal anesthetics in the rabbit. *Jour. Pharmacol. and Exper. Therap.*, 57: 221, 1936.
6. Bieter, R. N., McNearney, J. J., Cunningham, R. W. and Lenz, Oa. On the duration of spinal anesthesia in the rabbit. *Jour. Pharmacol. and Exper. Therap.*, 57: 264, 1936.
7. Braun, H. Ueber den Einfluss der Vitalität der Gewebe auf die ortlichen und allgemeinen Giftwerkungen Localanästhesirender Mittel und uber die Bedeutung des Adrenalins für die Localanästhesie. *Arcb. f. klin. Cbir.*, 69: 541, 1903.
8. Corning, L. Spinal anesthesia and local medication of the cord. *New York Med. Jour.*, 42: 483, 1885.
9. Co Tui, F. W. The intracisternal minimal lethal dose of procaine HCl in dogs. *Jour. Pharmacol. and Exper. Therap.*, 48: 223, 1933.
10. Co Tui, F. W. The effect of different narcotics and narcotic combinations on the minimal lethal dose of procaine HCl intracisternally. *Jour. Pharmacol. and Exper. Therap.*, 48: 229, 1933.
11. Co Tui, F. W. Further studies in subarachnoidal anesthesia. *Anestb. and Analg.*, 13: 143, 183, 1934.
12. Co Tui, F. W. and Standard, S. Experimental studies on subarachnoidal-anesthesia. *Surg. Gynec. and Obst.*, 55: 290, 1932.
13. Dunlap, J. G. The fate of procaine in the dog. *Jour. Pharmacol. and Exper. Therap.*, 55: 464, 1935.
14. Emmett, J. L. Subarachnoidal injections of procaine HCl. *J. A. M. A.*, 102: 425, 1934.
15. Ferguson, L. K. and North, J. P. Observations on experimental spinal anesthesia. *Surg. Gynec. and Obst.*, 54: 621, 1932.
16. Gasser, H. S. and Erlanger, J. The role of fiber size in the establishment of a nerve block by pressure or cocaine. *Am. Jour. Physiol.*, 88: 581, 1929.
17. Gerlough, T. D. The influence of *p*H on the activity of certain local anesthetics as measured by the rabbit's cornea method. *Jour. Pharmacol. and Exper. Therap.*, 41: 307, 1931.
18. Gros, O. Über die Narkotika und Localanästhetika. *Arcb. f. exper. Patb. u. Pbarm.*, 63: 80, 1910.
19. Gwinn, C. D. and Ferber, E. W. Relationship of hydrogen ion concentration to the efficiency and toxicity of local anesthetic solutions. *Jour. Am. Dent. Assn.*, 23: 1298, 1936.
20. Hatcher, R. A. and Eggleston, C. A contribution to the pharmacology of novocaine. *Jour. Pharmacol. and Exper. Therap.*, 8: 385, 1916.
21. Heinbecker, P., Bishop, G. H. and O'Leary, J. Allocation of function to specific fiber types in peripheral nerves. *Proc. Soc. Exper. Biol. and Med.*, 30: 304, 1932–1933.
22. Hertzler, A. E. The Technique of Local Anesthesia. C. V. Mosby Co., St. Louis, 1933, p. 21.
23. Hirschfelder, A. D. and Bieter, R. N. Local anesthetics. *Physiol. Rev.*, 12: 190, 1932.
24. Johnston, J. F. C. and Henderson, V. E. An experimental inquiry into spinal anesthesia. *Anestb. and Analg.*, 11: 78, 1932.

25. Knoefel, P. K., Herwick, R. P. and Loevenhart, A. S. The prevention of acute intoxication from local anesthetics. *Jour. Pharmacol. and Exper. Therap.*, 39: 397, 1930.
26. Koller, Karl. Ueber die Verwendungen des Cocain zur Anasthesirung am Auge. *Wien. Med. Wchnschr.*, 34: 1276, 1309, 1884.
27. Koster, H. and Weintrob, M. Complications of spinal anesthesia. *Am. Jour. Surg.*, 8: 1165, 1930.
28. Koster, H., Shapiro, A. and Leikensohn, A. Spinal anesthesia. *Am. Jour. Surg.*, 33: 245, 1936.
29. Lipschitz, W. and Laubender, W. Die pharmakologischen Wirkungen des Percain, eines neuen Lokalanaestheticums. *Klin. Wchnschr.*, 8: 1438, 1929.
30. Lundy, J. S. and Tovell, R. M. Annual report for 1935 of the section on anesthesia. *Proc. Staff Meet. Mayo Clinic*, 11: 421, 1936.
31. Lundy, J. S. Personal communication, quoted from, Hirschfelder, A. D. and Bieter, R. N. Local anesthetics. *Physiol. Rev.*, 12: 256, 1932.
32. Lundy, J. S. The conservative use of anesthetics. *South. Med. Jour.*, 29: 42, 1936.
33. MacDonald, A. D. and Israels, M. C. G. The estimation of the relative toxicities and efficiencies of local anesthetics. *Jour. Pharmacol. and Exper. Therap.*, 44: 359, 1932.
34. Mayer, E. The toxic effects following the use of local anesthetics. *J. A. M. A.*, 82: 876, 1924.
35. Munch, J. C. Bioassays. The Williams and Wilkins Co., Baltimore, 1931, p. 54.
36. Ockerblad, N. F. and Dillon, T. G. The use of ephedrine in spinal anesthesia. *J. A. M. A.*, 88: 1135, 1927.
37. Rous, P. and Drury, D. R. Outlying acidosis. *J. A. M. A.*, 85: 33, 1925.
38. Rudolph, R. D. and Graham, J. D. Notes on sulphate of ephedrin. *Am. Jour. Med. Sc.*, 173: 399, 1927.
39. Seevers, M. H. and Waters, R. M. Circulatory changes during spinal anesthesia. *Anesth. and Analg.*, 11: 85, 1932.
40. Serafin, F. J. A precaution in the use of procaine-epinephrine for regional anesthesia. *J. A. M. A.*, 91: 43, 1928.
41. Sollmann, T. Anesthesia of the human skin. *Jour. Pharmacol. and Exper. Therap.*, 11: 69, 1918.
42. Sollmann, T. Comparative activity of local anesthetics. *Jour. Pharmacol. and Exper. Therap.*, 10: 379, 1917–1918; 11: 1, 1918.
43. Sollmann, T. A Manual of Pharmacology, Fourth Ed. W. B. Saunders Co., Philadelphia, 1932, p. 334.
44. Tainter, M. L. Comparative actions of sympathomimetic compounds. *Arch. internat. de pharm. et de therap.*, 41: 365, 1931.
45. Tatum, A. L., Atkinson, A. J. and Collins, K. H. Acute cocaine poisoning, its prophylaxis and treatment in laboratory animals. *Jour. Pharmacol. and Exper. Therap.*, 26: 325, 1925–1926.
46. Tatum, A. L. and Collins, K. H. Acute cocaine poisoning and its treatment in the monkey. *Arch. Int. Med.*, 38: 405, 1926.
47. Winter, L. An experimental and clinical investigation of a new ischemic agent for use in local anesthetic solutions. *Dental Outlook*, 20: (Dec.) 1933.

REGIONAL ANESTHESIA: AGENTS AND METHODS*

JOHN S. LUNDY, M.D. AND EDWARD B. TUOHY, M.D.

Section on Anesthesia, The Mayo Clinic

ROCHESTER, MINNESOTA

THE use of regional anesthetic agents and methods has facilitated operation on many patients, both to the benefit of the surgeon and the patient. In considering the use of these agents and methods, those that are of special value will be discussed and only mention will be made of some of the others.

In the first place we consider procaine, also called novocain or neocaine, the most valuable of all of the local anesthetic agents because of the relative freedom from producing untoward results with which its use is attended. It has certain deficiencies, however, one of which is that it is not a good surface anesthetic; accordingly, other agents have been synthesized for this purpose. One of them is a drug called pontocaine. This drug, in addition to being a surface anesthetic, is capable of producing prolonged local and spinal anesthesia. It is about ten times as potent, and therefore ten times as toxic, as procaine.

The next drug is known in Europe as percaine and in this country as nupercaine. It, too, is ten times as potent and ten times as toxic as procaine. It produces prolonged periods of anesthesia and is a surface anesthetic. Of the two, we prefer pontocaine to nupercaine, because nupercaine is essentially a derivative of quinine, and derivatives of quinine are more toxic to the heart than is procaine.

The next drug varies greatly in chemical composition from nupercaine and from procaine and pontocaine. It is called metycaine, and next to procaine we think it is the most promising, because it will produce surface anesthesia, local anesthesia and spinal block anesthesia. It is not as toxic as nupercaine or pontocaine, but its effect lasts a little longer than that of procaine. Metycaine is of a very different chemical structure from procaine. Occasionally one will find that a dentist who cannot use procaine, because he gets a rash when he does employ it, can use metycaine.

Vasoconstrictors are those drugs which so often are used to advantage in connection with local anesthetics. One is epinephrine, or adrenalin, another ephedrine, and the third cobefrin. The formulas are very similar, and there is also considerable similarity in the physiologic effect of these agents. The effects of epinephrine last about fifteen minutes, and if it is pure and fresh it does not have certain undesirable vagus influences. The effects of ephedrine last about forty-five minutes, and it is therefore more useful in connection with spinal anesthesia than is epinephrine, except when the blood pressure does not respond readily, in which case one can then use ephedrine and epinephrine alternately. When the blood pressure is extremely low these drugs should be given intravenously rather than intramuscularly or subcutaneously. In extreme cases these drugs might be used intraspinally, for that method is said to be the most effective.

From the standpoint of local hemostasis, epinephrine is the most useful of the agents for admixture with a solution of a local anesthetic for infiltration of tissue. Ephedrine does not satisfy the demands in this particular phase of local anesthesia. On the other hand epinephrine is not the equal of ephedrine for sustaining the blood pressure during spinal anesthesia. For hemostasis, cobefrin is the equal of epinephrine but

* Part of symposium read before the Philadelphia County Dental Society in collaboration with the Philadelphia County Medical Society, Philadelphia, Pennsylvania, November 22, 1935. Also read before the meeting of the Post Graduate Medical Assembly of South Texas, Houston, Texas, December 3 to 5, 1935.

not of ephedrine. It has been demonstrated by one of us (Tuohy) that ephedrine and cobefrin can be given by mouth, but that fact is not of particular interest from the standpoint of local anesthesia. It is important not to administer these drugs in large doses.

The barbiturates are of real advantage in connection with local and regional anesthesia, in that they bring the patient to a condition wherein he is not apprehensive and wherein he manufactures within his body little more than the normal amount of epinephrine. In addition, the barbiturates are specifically antispasmodic, and in this way protect the patient against one of the most disastrous effects of the local anesthetic agent. When given intravenously in soluble form, they may be used as a rather specific antidote for most of the local anesthetic agents in really controlling convulsions once they have appeared. Morphine and other analgesics are of benefit to the patient because they minimize the amount of pain associated with the introduction of the needle into the unanesthetized tissue and lower the patient's metabolic rate so that he does not destroy procaine as rapidly as he otherwise would.

We have done some experimental work on animals concerning the effect of these drugs in connection with spinal anesthesia. When the spinal anesthetic was given the blood pressure and pulse pressure were decreased markedly. After a time ephedrine was given subcutaneously and the spot where it was injected was massaged. There was a gradual increase in the pulse pressure, then an increase in the blood pressure, and this was followed by a further increase in the pulse pressure.

In another experiment, when the spinal anesthetic was administered there was a decrease in blood pressure. When ephedrine was given there was a gradual increase in blood and pulse pressures. Then the spot where the ephedrine was injected was massaged and the result was a second effect, as though another dose had been given. When the vagus nerves were cut on each side, the high pulse pressure disappeared. It seems, then, that there must be as definite an effect on the vagus nerves from using ephedrine as is apparent when impure epinephrine is used.

In still another experiment a tracing of the normal blood pressure was made and a spinal anesthetic was then given. There was a fall in blood pressure. When ephedrine was administered and the site of injection was massaged, there was a gradual increase in blood pressure together with a gradual increase in pulse pressure. Then atropine was given to paralyze the vagus nerves and there was a definite change in the volume of the pulse pressure. It is evident, then, that when the vagus nerves are cut or when they are paralyzed with atropine, the pulse pressure becomes less than when an increased pulse pressure has been produced by the previous administration of ephedrine without atropine.

We also noted the experimental effect of procaine on the femoral blood pressure. When a small dose of procaine was given intravenously, transient depression of the blood pressure appeared; this might be called a slight reaction of procaine. Marked depression of the blood pressure was produced by repeated injections of a dose which, if given only once, would have caused only a slight reaction. The effect of giving repeated small doses was the equivalent of the effect of one large dose given slowly.

A review made at The Mayo Clinic disclosed that in a period of four years the number of patients who were given local anesthetics was greater than the number who were subjected to any other one agent or method of anesthesia. When we set apart from the whole number of patients anesthetized those for whom "special" agents or methods were used and then distributed those patients again on the basis of whether local or general agents were employed, we observed that in the majority of cases irrespective of whether a general anesthetic had been given a local anesthetic had been employed. That means

that when a patient, because of the lesion for which he is to be operated or because of additional lesions that increase the risk of operation for him, or for any other reason, is recognized as a subject for whom a special agent or method should be employed, the probabilities are great that a local anesthetic agent will be used, either alone or in combination with some general anesthetic agent, such as one of the gases.

Various methods of block anesthesia are employed at the clinic. Of these, we find brachial plexus block the most difficult to use; that is, with this method it is most difficult to obtain satisfactory anesthesia in a high percentage of cases. If the needle happens to strike the nerve trunks, the resulting block is satisfactory. Too often, however, the desired paresthesia of the hand does not appear when the needle is inserted into the tissues of the neck, and it then becomes a matter of guess work whether the local anesthetic solution will spread far enough in the cervical tissues to include the brachial plexus. Accordingly, the method is not used very frequently at the clinic although our results might be better if we had had more practice with it.

Cervical block is used in a certain number of cases, but not in as large a number now as before Magill's intratracheal method of administering a general anesthetic became available. Cervical block is now used principally for patients who are to have an operation on the neck and who are unsuitable for general anesthesia.

It is of definite advantage to the surgeon to have the line of incision or the field of operation infiltrated, as for instance for operations on the abdominal wall or the neck, even when a general anesthetic is to be used. When such infiltration is performed, the operative field will be drier than otherwise because of the hemostasis effected by the local anesthetic and by the epinephrine.

Field block and infiltration of tissue is performed year in and year out because this procedure affords good anesthesia in a high percentage of cases. Sacral block is frequently done because in the clinic many operations are performed for anal and rectal conditions. This method of block provides anesthesia with a minimum of untoward results. It provides relaxation without much prostration, and it avoids the distortion of the anus that results from infiltration. For anal operations sacral block is without doubt the best method of anesthesia. This has been especially true since various preparations have been developed which are useful for preliminary medication, particularly pentobarbital sodium, or nembutal. Use of these preparations adds to the comfort of the patient when sacral block and anal operations are to be performed.

Spinal anesthesia is used frequently and with considerable satisfaction, but it is not used when the patient is markedly debilitated. The dose for the average adult is about 1 mg. per pound of body weight, and the total dose does not exceed 200 mg. in any case; in the average case the dose is either 120 or 150 mg. The site of injection is usually one of the lumbar interspaces. The space between the first and second lumbar vertebras is selected for operations in the upper part of the abdomen; the space between the second and third, for operations in the midportion of the abdomen, and the space between the third and fourth, for operations on the thigh, perineum, groin or bladder. The solution should be driven slowly from the syringe into the spinal fluid, maintaining a constant speed of injection in all cases. We inject 0.5 c.c. of solution per second. Variations from this should be in the direction of still slower injection; the solution will occupy as many cubic centimeters of space subdurally as it occupied in the syringe regardless of how slowly it is injected because the fluid is not compressible. If it is injected too rapidly, in some cases the solution of procaine will travel as a stream through the spinal fluid to more distant points than it should, especially if the amount of spinal fluid is scanty and as a

result is under low pressure. We do not use barbotage.

The volume of diluent in the syringe in which procaine has been dissolved bears directly on the duration of anesthesia and on the degree of relaxation that is to be expected following injection of the anesthetic into the spinal fluid. Anesthesia is longer with a concentrated solution than when a more highly diluted solution is used. For example, if 150 mg. of procaine are delivered from a syringe that contains 5 c.c. of solution, the material injected is 5 c.c. of a 3 per cent solution. If 150 mg. of procaine is dissolved in only 3 c.c. of solution in the syringe, then the material injected is 3 c.c. of a 5 per cent solution. The anesthesia resulting from injection of the 5 per cent solution lasts longer and produces more relaxation or paralysis than that produced by the 3 per cent solution. If a 10 per cent solution is injected, there is danger of injury to the spinal cord. Experimentally, lesions in the spinal cord of the dog can be produced by injecting a sufficiently large dose of procaine in a sufficiently strong concentration. Such lesions develop, however, only following the administration of large doses. The concentrations ordinarily used to produce spinal anesthesia are, for the average individual, relatively safe. When lesions are produced experimentally, the animals are permanently and fatally paralyzed, and the pathologist always finds the lesion. The four main points to be remembered in administering a spinal anesthetic agent are, then: the dose, the rate of injection, the site of injection, and the volume of solution in the syringe.

Some of the untoward symptoms that develop in the course of spinal anesthesia probably occur because procaine is very quickly absorbed from the spinal fluid and, if it reaches a sufficient concentration in the blood stream, it is sure to produce certain systemic effects such as nausea, vomiting, exaggeration of the fall in blood pressure, and perhaps other symptoms which are not yet recognized as being attributable to this systemic effect. According to Nowak, decomposition products of procaine appear in the urine in twelve minutes after this agent has been injected into the spinal fluid. It is rather commonly observed that nausea following the spinal injection of procaine also appears on the average in about twelve minutes. The most marked fall in blood pressure appears, on the average, about twenty-two minutes after the subdural injection of procaine. These occurrences coincide with our belief that part of the untoward result from spinal anesthesia is attributable to the presence of procaine in toxic quantities in the circulating blood. On the basis of such a belief we have decreased the concentration of the solution injected to 3 per cent, but not lower because with less than a 3 per cent solution relaxation in most cases is not obtained. In order to interfere, too, with the absorption of procaine from the spinal fluid, we have purposely tried to lower the blood pressure of the average adult during spinal anesthesia to about 80 or 90 mm. of mercury systolic. At the same time we have not wanted to have the blood pressure fall to the extreme degrees that are observed when ephedrine is not used and large doses of procaine are given. Therefore we give ephedrine; but in order that the blood pressure will not rise enough to defeat our purpose in lowering it to some extent, we have given doses of 25 rather than 50 mg. of ephedrine to the average patient. If more ephedrine is needed because of a subsequent fall in blood pressure to perhaps 50 mm. systolic, we administer all or part of 25 mg. of ephedrine intravenously during the period when the blood pressure is low, trying to raise the pressure to about 85 mm. systolic. To repeat, our hope, then, is to decrease the efficiency of the circulation of blood so as to decrease the rate of absorption of procaine from the spinal fluid, but we also wish to prevent the blood pressure falling to a dangerously low level. Procaine that reaches the blood stream is destroyed by the liver, as was shown by the work of

Eggleston and Hatcher. Their work was reviewed and confirmed by Dunlop.

Spinal anesthesia is indicated when relaxation is desired, but general anesthesia, such as that produced by ether, is contraindicated. Spinal anesthesia, like other methods of anesthesia, should be chosen when it is indicated rather than used routinely. In any event the important thing is not to administer a spinal anesthetic to a patient when there is doubt as to its safety for the particular patient. The uses and abuses of spinal anesthesia could be discussed at great length; the literature contains not less than 3500 to 4000 articles on the subject of spinal anesthesia.

Splanchnic anesthesia, effected through the posterior approach of Kappis, has not been sufficiently satisfactory (successful in 48 per cent of cases) to warrant using it except in unusual cases. The method of blocking the splanchnic nerves after the abdomen has been opened has been very useful in the hands of many men, but it has not been as widely used as it should be.

When block anesthesia of a digit is desired, a wheal is made on the dorsum of the member and injections are made around the finger at some point proximal to the site of operation. If one injects intradermally and subcutaneously, from skin to bone, and then injects through the hand to the palmar surface but not into it, good anesthesia results. The entire hand can be anesthetized by using a bracelet type of block at the wrist, injecting a 1 per cent solution of procaine directly on the surface of the median nerve; that the needle has reached the median nerve will be evident if paresthesia is obtained. Similar injection is made on the surface of the ulnar nerve. Also, a 1 per cent solution of procaine is deposited in the region of the branches of the radial nerve. The balance of the block can be accomplished with 0.5 per cent solution of procaine.

The whole foot can be blocked off by using a bracelet block at the ankle, and by injecting 1 per cent solution on the surface of the posterior tibial and anterior tibial nerves; again an attempt should be made to produce paresthesia with the needle before the injection is finished. For operations on the great toe, the toe is isolated from the rest of the foot by block anesthesia produced by an L-shaped injection. The needle is passed from the dorsal surface of the foot against, but not into, the plantar surface. This injection is so satisfactory for the Mayo bunion operation that orthopedic surgeons at the clinic seldom perform the operation with any other method of anesthesia. The innervation of the great toe differs slightly from that of the other digits, so that one must be sure to inject thoroughly from the skin of the dorsum of the foot to the skin of the plantar surface at all points except through the bone. Bone can be removed from the tibia, to be implanted in the spinal column, by using a field block that includes intradermal and subcutaneous injection and the injection of the periosteum. The entire leg below the knee can be anesthetized by injecting, from skin to bone, all the way around the leg. This is, however, a tedious method of injection and is somewhat painful to the patient, sometimes requiring large amounts of procaine.

For operations on the knee joint a diamond-shaped type of field block can be effected, 10 to 30 c.c. of procaine-epinephrine solution being injected beneath the patella. The resulting anesthesia, however, is not always satisfactory.

For the treatment of old fractures, infiltration must be carried down to the periosteum on both sides of the fracture and all the way around the fractured bone. However, for acute or recent fractures, and in the presence of a hematoma, a 2 per cent solution of procaine can be used. When the needle has entered the hematoma, which can be determined by aspirating some blood from it, the solution should be injected slowly; it will dissipate itself through the blood clot and provide anesthesia for the reduction of the fracture.

For operations on the neck deep block anesthesia is satisfactory. The needles are

inserted in such a manner that they point caudally rather than toward the head or at right angles to the skin. They are directed so that their points rest on the tips of the transverse processes of the second, third and fourth cervical vertebras; against these transverse processes, on each side, about 25 c.c. of a 1 per cent solution of procaine and epinephrine is injected. The injection of the solution against a transverse process of the second cervical vertebra may result in an untoward reaction if the needle happens to enter a blood vessel. Aspiration should be performed before injection is begun to determine whether the tip of the needle is in a blood vessel. Injection should always be slow because of the occurrence, although infrequent, of unconsciousness and mild tonic convulsions when the anesthetic solution has been introduced into a blood vessel. Slow injection allows the untoward signs to develop before much of the solution has been injected. If they do develop, injection can be discontinued and the needle moved.

Superficial cervical block also provides good anesthesia and can be performed very simply by infiltrating the tissue which lies between the skin of the neck and the superficial surface of the sternocleidomastoid muscle.

For operations on the thyroid gland, a dry field is obtained by infiltrating the skin and subcutaneous tissues overlying the gland. However, it is possible to operate on the thyroid gland without infiltration. Deep and superficial cervical block can be used together, or superficial block alone can be used and a small amount of procaine solution can be infiltrated into the tissues when the gland has been exposed. The Bartletts have advocated that infiltration be avoided and their method of injection be employed.

For intracranial operations, that portion of the scalp in which the superficial incision is to be made can be blocked off by infiltrating the area usually covered by the hatband. If a limited portion of the scalp is to be blocked, this area can be circumscribed by infiltration of the local anesthetic agent; such a method of anesthesia is known as "field block." The technical points in block for cranial operations are to infiltrate three distinct layers separately. The intradermal injection blocks the superficial layer, the subcutaneous injection blocks the layer between the skin and the cranium, and the injection against the bone blocks the periosteum. The solution used is 0.5 per cent procaine and epinephrine. When the operation is in or near the temporal region, the periosteum of the temple is infiltrated from above downward.

For operations on the breast, the pedicle of the breast should be narrowed by mechanical means and injection made into the narrowed pedicle. If an assistant is not available, some device can be used, such as a clamp, to narrow the pedicle of the breast. On being released after injection, the tissue of the breast carries with it the solution of procaine, and the breast is then isolated from the chest by a layer of solution. Any operation that is included within the area of anesthesia, even including simple amputation, can then be performed.

In the posterior method of splanchnic block, injection is bilateral. On each side a point is found about 8 cm. lateral to the spinous process of the first lumbar vertebra and two finger breadths (3 cm.) below the lower border of the twelfth rib. The needle is inserted through that point directly against the lateral surface of the body of the first lumbar vertebra, and then, by a process of feeling the bone with the bevel of the needle, and pushing the needle in a little and again feeling, the point of the needle is thrust into a plane that would just touch the anterior surface of the body of the vertebra. At that point from 25 to 50 c.c. of either 0.5 or 1 per cent solution of procaine is injected. In about 50 per cent of cases a considerable part of the intra-abdominal region will be anesthetized. However, the cecum and appendix are often not satisfactorily anesthetized and in many cases operation cannot be continued without pain in the region of these

structures unless paravertebral injection of the right tenth thoracic space has been done. Abdominal wall block must be used, of course, in addition to splanchnic block for abdominal operations. The abdominal wall can be infiltrated and blocked so that an incision can be made and the abdominal cavity opened. For operations in the upper part of the abdomen, the abdominal wall can be infiltrated along the costal margin and down the lateral border of the rectus muscles. For operations on the bladder, the injection of the abdominal wall is diamond shaped, extending from the umbilicus to the symphysis pubis. For hernia, the injection is made on a line from the antero-superior iliac spine toward the umbilicus.

In articles on regional anesthesia the raising of the intradermal wheal is not sufficiently emphasized. The bevel of the needle should not be turned upward, as is described in some textbooks, but downward, against the skin. The left index finger should pull the skin toward the needle, while the right hand, holding the syringe, forces the needle against the skin. Pressure should be maintained on the plunger of the syringe all the while so that the moment the edge of the bevel of the needle is buried in the most superficial layer of the skin the wheal will start to form. Injection should not be delayed until the entire end of the needle is buried in the deep layers of the skin. If the method we have advocated is employed, the minimum of pain is caused.

In sacral block, after the wheal has been raised, the skin over the sacrum is immobilized with the left hand and the point of the needle, already attached to the syringe, is passed into the sacral hiatus, with the bevel of the needle against the bone. The anesthetist rests the hand which holds the syringe on the patient's buttock so that, should the patient move, the anesthetist's hand will be raised and the needle will follow the hand rather than the hand following the needle, probably breaking the needle. The first part of the procedure is performed with a short needle. After the short needle has been introduced into the caudal canal and after 2 or 3 c.c. of a 1 per cent solution of procaine have been injected, the needle is withdrawn and another needle, with its stilet in place, is introduced. This needle must be so inserted that its bevel will lie on the rough surface of the bone, if it is to be advanced easily into the caudal canal. Its point should be inserted no further cephalad than a line between the second sacral foramina. Higher insertion of the needle may result in subdural injection, for the tip of the dural sac may be pierced by the caudal needle. If the sac is perforated by the needle the hole does not close for several days. If the ordinary amount of solution, 30 c.c., is injected into the caudal canal, thirty minutes will be required to produce anesthesia in the average case. If more relaxation or quicker anesthesia must be produced, the procedure just outlined can be supplemented by injection of anesthetic solution into the first four sacral foramina on each side. If anesthesia has not been satisfactory, and if thirty or forty-five minutes can be allowed for the drug to saturate the nerve trunks, larger amounts of solution can be injected into the caudal canal. Anesthesia then will often result, and the more solution that is injected into the canal the more widespread will be the field of anesthesia. If time does not permit for anesthesia to become established by the caudal injection, then it may be combined with injection into the second sacral foramina.

If it is desired to produce anesthesia of the vulva, injection of the perineal nerves on each side can be achieved by inserting the needle mesial to the tuberosities of the ischia on each side and on a level with the posterior border of the anus. The tip of the needle is inserted to a depth of about 1 inch (2.5 cm.) and at that point 15 to 25 c.c. of 1 per cent solution of procaine and epinephrine is injected. This will produce anesthesia and relaxation for obstetric procedures or for minor operations on the labia.

Advantage can be taken of the various methods of regional anesthesia for purposes of diagnosis, prognosis, or treatment of painful conditions to the benefit of both patient and physician. However, this is so large a field that it cannot be discussed here.

SUMMARY

Procaine in our experience has been the most valuable of all the local anesthetic agents. It is used extensively for spinal anesthesia and other types of regional anesthesia such as sacral block, cervical plexus block and abdominal wall block. Vasoconstrictor drugs such as epinephrine and cobefrin are used to prolong the action of procaine, and ephedrine is used in spinal anesthesia to help sustain blood pressure. Barbiturates are administered prior to use of procaine because of their sedative and antispasmodic action. The technique of spinal anesthesia and numerous regional anesthetic procedures are described, and the indications for such methods are stated.

REFERENCES

Bartlett, Willard and Bartlett, Willard, Jr. A safe and satisfactory method of anesthesia for toxic goiter patients. *Surg., Gynec. and Obst.*, 58: 737–740 (Apr.) 1934.

Dunlop, J. G. The fate of procaine in the dog. *Proc. Staff Meetings of Mayo Clinic*, 9: 241–244 (Apr. 18) 1934; also, *Jour. Pharmacol. and Exper. Therap.*, 55: 464–481 (Dec.) 1935.

Eggleston, Cary and Hatcher, R. A. A further contribution to the pharmacology of the local anesthetics. *Jour. Pharmacol. and Exper. Therap.*, 13: 430–487 (Aug.) 1919.

Kappis. Quoted by Hewer, C. L. Recent Advances in Anesthesia and Analgesia. Philadelphia, P. Blakiston's Son and Company, 1932, pp. 106–108.

Magill, I. W. Endotracheal anesthesia. *Proc. Roy. Soc. Med., Section of Anesthetics*, 22: 83–88 (Nov. 2) 1928.

Nowak, S. J. G. The urinary excretion of novocain after spinal anesthesia and the theory of toxic absorption. *Anesth. and Analg.*, 12: 232–242 (Nov.-Dec.) 1933.

Tuohy, E. B. A comparative study of the physiological activity of cobefrin and epinephrine. Unpublished data.

SPINAL ANESTHESIA

MEYER SAKLAD, M.D.

Assistant Anesthetist, Rhode Island and Memorial Hospitals; Anesthetist, St. Joseph's, Charles V. Chapin, Providence Lying-In and Miriam Hospitals

PROVIDENCE, R. I.

IN considering the present status of the many aspects of spinal anesthesia one is impressed with the increasing agreement among anesthetists of its many formerly disputed phases. Methods are being standardized, greater stress is being laid upon the details of technique; indications and contraindications are understood more definitely and clearly.

An attempt is made in this paper to consider the various angles of the subject necessary to familiarize one with the several agents and procedures of the method. It is only through an exact knowledge of a procedure that it can be applied with best results and greatest safety.

AGENTS

The most popular agents in spinal anesthesia, in their probable order, are: procaine, pontocaine, nupercaine and metycaine. Though comparatively small amounts of these drugs are employed in this type of anesthesia the question of relative toxicity must not be overlooked. In a previous communication[27] this aspect was considered. Based on animal experimentation in which the comparative fatal intravenous dose was determined and the relative dosage considered, a corrected toxicity ratio, as compared to procaine, was reached. Thus, in the work of Nowak, as quoted by Marvin,[22] and of Wiedhopf,[33] giving procaine unity, we find the corrected toxicity ratio as listed in Table I.

Wiedhopf did not consider metycaine. To accept entirely this ratio as the true relative toxicity of these drugs would not be fair for it must be understood that this work was not done on human beings and that the other factor, relative dosage, may be justly disputed. Clinically, Lundy[18–20] feels that procaine is the safest of the agents. Employing this drug he feels that there is a wide margin of safety between failure of respiration and failure of the heart. Nupercaine, he holds, offers very little margin of safety between respiratory and cardiac failure.

TABLE I
CORRECTED TOXICITY RATIO
(As compared to procaine)

	Nowak	Wiedhopf
Procaine	1.0	1.0
Pontocaine	0.58	0.71
Nupercaine	0.71	0.958
Metycaine	1.36	

These agents vary also as to duration of action, and, as given by Marvin,[22] are: procaine, one hour; metycaine, ninety minutes; pontocaine, two hours and nupercaine three hours.

Various neurologic changes following spinal anesthesia have been reported.[1,3,17,24] Lundy and others[21] showed that neurologic changes did not follow intraspinal injection of drugs of therapeutic doses. Others[11,16] have shown that changes, when they do occur, are transitory.

The agents, in different dosages and combinations, vary also as to their specific gravities. With the present dependence, to a large degree, on the difference in gravity between the agent and spinal fluid to limit or extend the height of anesthesia, a knowledge of these relative gravities is important. They may be found listed in Tables II and III.

The specific gravity of the average spinal fluid is 1.007; it is important that we do not forget that spinal fluid may have a

specific gravity anywhere between 1.001 and 1.010.[14] Thus, of the solutions of agents themselves, we have but the 1:1500 solution of nupercaine in water which we may consider as consistently lighter than normal spinal fluid. This solution is unstable and is not employed. The 1:1500 solution of nupercaine in 0.5 per cent saline (Jones solution) has been considered a hypobaric one. It is true that spinal fluid, with gravities of less than 1.003 might be rare but they must be considered to exist; therefore it must not be forgotten that this solution in such a spinal fluid is hyperbaric.

TABLE II
SPECIFIC GRAVITY OF SOLUTIONS OF PROCAINE AND PONTOCAINE

Procaine HCl Mg.	Pontocaine 1 Per Cent in Saline,* Mg.	Dextrose 10 Per Cent, C.c.	Spinal Fluid S.G. 1.007, C.c.	Specific Gravity
200	..	...	2.0	1.025
200	..	...	4.0	1.013
200	..	...	8.0	1.008
50	..	0.5	2.0	1.015
100	..	0.5	2.0	1.018
100	..	0.5	4.0	1.014
150	..	0.5	4.0	1.0155
50	..	1.5	2.0	1.021
100	..	1.5	2.0	1.023
100	..	1.5	4.0	1.017
150	..	1.5	4.0	1.019
...	10	1.0	2.0	1.014
...	10	0.5	2.5	1.011
50	10	...	3.0	1.009
50	15	...	2.5	1.009
50	20	...	2.0	1.009
...	10	0.5	...	1.016
...	10	1.0	...	1.020

* As commercially distributed with specific gravity of 1.007.

One per cent pontocaine in saline for spinal anesthesia, as commercially distributed, has a specific gravity of 1.007, or that of the average spinal fluid. Thus it might be lighter than some spinal fluids and heavier than others.

A solution with a specific gravity lighter than spinal fluid injected into the subarachnoid space may be expected to give a different result than the use of one which is heavier than the medium in which it is placed. Thus, in a patient placed on his back immediately after intraspinal injection, a heavy solution will result in a higher level of posterior, or sensory, anesthesia than anterior, or motor. A solution lighter than spinal fluid, with the patient in the same position, will find its way higher on the anterior aspect of the canal and cause a higher level of motor paralysis than of sensory. A high level of sensory anesthesia, of itself, is not to be feared. A high anterior, or motor, block is to be feared and prevented. The higher the motor block the greater the extent of respiratory involvement.

TABLE III
SPECIFIC GRAVITY OF SOLUTIONS OF METYCAINE AND NUPERCAINE

Agent	Solution	Specific Gravity
Metycaine.....	1:20 in 0.9 per cent saline	1.020
	1:10 in 0.9 per cent saline	1.036
Nupercaine.....	1:200 in 0.5 per cent saline	1.0046
	1:1500 in 0.5 per cent saline	1.0030
	1:1500 in 0.9 per cent saline	1.0061
	1:1500 in water	1.00005
	10 per cent procaine in 1:200 nupercaine	1.018

These agents vary also as to the degree of their effect on blood pressure. Pontocaine seems to have a less depressive action than procaine. Figures 1 and 2 are composite charts showing the systolic pressures in 20 consecutive cases of anesthesia under each of these agents. No effort was made to run a parallel series and subsequent investigation might prove our present contention to be wrong. Some workers feel that the effect of nupercaine, intraspinally, on blood pressure is not quite as great as that of procaine.

PREMEDICATION

A moderate dosage of a barbiturate given the night before operation is of value. Medication in the morning before operation should be individualized. No routine dose should be employed. The type of operation, mental attitude and condition of the patient should all be taken into

consideration. Too heavy medication is as little to be desired as too light. The patient to be operated under any method of regional anesthesia is entitled to sufficient medication to dull his acute senses. For patients in good condition moderate dosage with morphine and scopolamine one hour preceding operation and the administration of a short lasting but rapidly acting barbiturate as pentobarbital or evipal given by mouth one-half hour before going to surgery is advisable. Though it is true that the barbiturates act as prophylactic agents to reaction from the local anesthetic drugs by virtue of their antispasmodic action, it is not for that purpose that they are employed as a premedication to spinal anesthesia. The convulsive attack due to an idiosyncrasy to or overdose by an anesthetic agent, in other types of regional anesthesia, is not a complication likely to occur during spinal anesthesia. It is only for their sedative action that they are employed before this form of anesthesia. It is interesting to note that CoTui[7] has shown that "small but effective doses of morphine, morphine-scopolamine and morphine-avertin given prior to cisternal injections (of procaine) do not cause a determinable decrease in the minimum lethal dose of the drug while the larger doses do, and that sodium amytal narcosis, whether light or profound, produces a marked reduction."

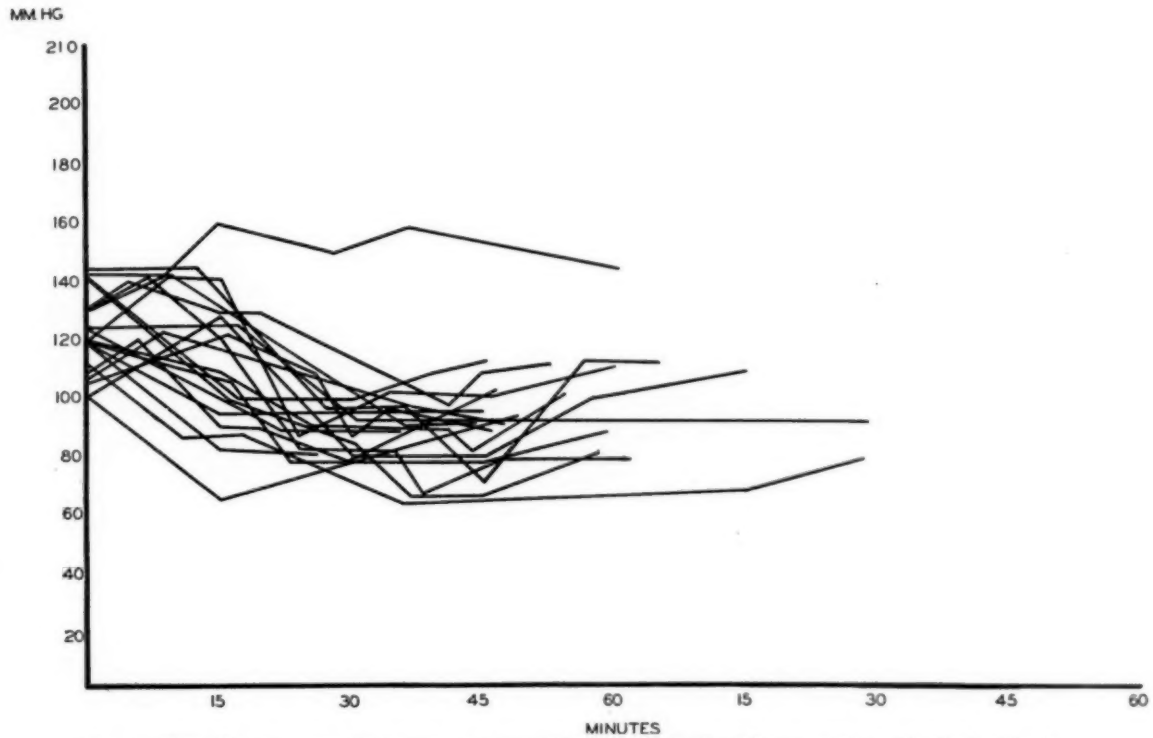


Fig. 1. Systolic pressures in twenty consecutive cases of ephedrine-procaine spinal anesthesia.

The time factor is important in preliminary medication. It requires from forty-five minutes to one hour for the full effect of morphine to become apparent, when given subcutaneously. It is for this reason that morphine is best given one hour preceding operation rather than fifteen to thirty minutes before the induction of anesthesia. In doing this, the occasional patient susceptible to morphine and exhibiting respiratory depression will be recognized before the anesthesia procedure is instituted. The administration of some other type of anesthesia or postponement of the operation will serve to prevent the marked depression that might occur had

the depressive action of morphine been allowed to manifest itself in the presence of an already depressed respiration during spinal anesthesia.

Some anesthetists routinely employ atropine as a premedicant. The reader is referred to the paragraph on ephedrine in regard to the combined action of atropine and ephedrine. If the patient is suffering from abdominal distention atropine is probably best omitted because it interferes with the function of the myoneural juncture of nerves which supply non-striated muscle fibres.[31]

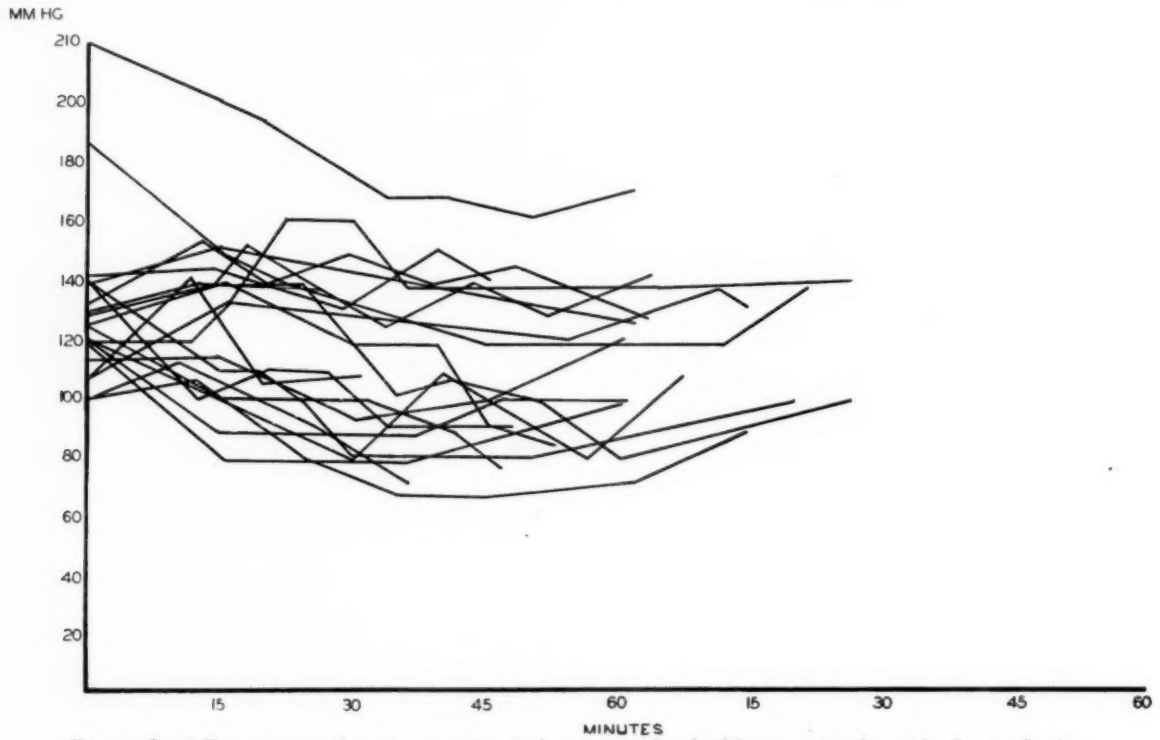


FIG. 2. Systolic pressures in twenty consecutive cases of ephedrine-pontocaine spinal anesthesia.

EPHEDRINE

Because it is fairly generally agreed that a fall in blood pressure, if severe, can result harmfully, the administration of a vasopressor drug before spinal anesthesia is almost universal. The drug employed by most anesthetists is ephedrine. CoTui[8] feels that ephedrine is considerably more efficacious in maintaining blood pressure than either saline infusion or transfusion. In employing a technique where the action of the anesthetic agent is to be limited to the perineum, as anal, vaginal or transurethral surgery, the administration of ephedrine may be omitted.

Because of the variation in speed of absorption of this drug from subcutaneous tissue and the impossibility of knowing beforehand the exact amount of ephedrine necessary to maintain the blood pressure at a satisfactory level in a given patient, Solkow[30] adds the ephedrine to 100 to 200 c.c. of saline and begins to administer this infusion intravenously immediately after the induction of spinal anesthesia. He controls the speed of flow of this ephedrine solution as to the level of blood pressure. Patients with arteriosclerosis frequently show poor response to the administration of ephedrine subcutaneously. By the intravenous drip method better control over their blood pressure is exhibited, according to Solkow.

It is important to know that the action of ephedrine is not entirely beneficial. That

ephedrine can cause cardiac irregularity is well known. Seevers and Meek[28] in laboratory experiments have shown that previous digitalization of the dog does not greatly alter the irregularity produced by ephedrine although there appears to be a tendency to increase the number of irregularities of ventricular type. In every case the irregularities continued through a longer time period, usually an increase of over 100 per cent. They feel that, "The cerebral and metabolic stimulation produced by ephedrine would under any circumstances be an objection to its use in heart disease."

Chen and Schmidt[5] have shown that ephedrine might cause heart failure even in the small dose of 1 mg. per kilo if given after a prolonged period, thirty minutes, of low blood pressure. Apparently a heart depressed by continued low blood pressure with consequent inadequate coronary flow is more sensitive to the depressant action of ephedrine and less responsive to its stimulant effect than the normal heart. It is therefore very dangerous in severe shock.

Meek and Seevers[23] have shown that if ephedrine is given after atropine the reflex effects are eliminated and tachycardia follows immediately. Atropine hastens and intensifies the pressor effect of ephedrine but shortens its duration. It has also been shown[23] that the barbiturates give a high degree of protection against the cardiac effects of ephedrine.

It has been demonstrated [2,32] that ephedrine can cause urinary retention. Colwell[6] has shown that continued intravenous administration of epinepherine interferes with and may even abolish the combustion of dextrose, possibly by suppressing the action of insulin. Because of the close similarity of action, between the above drug and ephedrine, it is likely that the same effect might follow similar administration of this latter drug.

METHODS

Before attempting to give a spinal anesthesia the anesthetist should appreciate the fact that the two most feared complications of this method are respiratory paralysis and severe fall in blood pressure. The higher the anesthesia the more nearly is respiratory paralysis approached and the greater is the fall in blood pressure. So-called perfect spinal anesthesia for every type of intra-abdominal surgery may be accomplished by the use of large dosage and volume. This is not good anesthesia. One of the qualities of a good anesthetist is his ability to limit the upward extent of the anesthetic solution consistent with the height of anesthesia desired for the type of surgery contemplated. With cyclopropane readily available one is justified in erring on the conservative side in administering anesthesia for upper abdominal surgery, particularly in poor risk patients.

The inguinal region receives its sensory supply from the twelfth thoracic nerve. The area about the umbilicus receives its nerve supply from the tenth and the area about the ensiform from the seventh thoracic nerve. Satisfactory anesthesia for upper abdominal surgery must extend to and involve the nerves coming from the fifth thoracic segment since the upper recti receive their motor innervation from this level. The fifth thoracic supplies sensation to the nipple line. Thus all upper abdominal surgery calls for anesthesia to this area. Anesthesia above the fifth thoracic not only increases the height of intercostal paralysis but begins to involve the cardiac nerves, the origins of which are in the first, second, third and fourth thoracic segments. It is true that it is difficult to stop the upward diffusion of an anesthetic agent at a set level but an attempt should be made to prevent too high an anesthesia.

The spinal cord ends at the level of the second lumbar vertebra. Punctures performed above this point may result in cord injury. Appreciation of these principles will do much to prevent many of the accidents that have occurred as the result of this form of anesthesia.

The factors which control the height of anesthesia: dosage, volume, site of injection, speed of injection, specific gravity and

position of patient are variable and, as one can see from the accompanying tables on technique, are differently employed by various anesthetists. In employing these tables to choose the proper dose of a drug necessary to give a certain level of anesthesia, one should remember that these tables are for guidance only. The patient's condition should be taken into consideration and the dosage based upon that. Anesthetic judgment should come into play fully as much in spinal anesthesia as in any other form.

TABLE IV

PROCAINE TECHNIQUES

	Perineum	Lower Abdomen	Mid Abdomen	Upper Abdomen	Remarks
Labat.					
Dose in mgm.	100	120	120	150	
Ephedrine in mgm.	0	0	0	0	
Dilution in c.c.	3	5	5	5	Approximate
Trendelenburg.	+	+	+	+	Immediate.
Site of puncture.	L_3	L_2	L_1	D_{12}	
Evans.					
Dose in mgm.	60	100	120	120	
Ephedrine in mgm.	0	0	0	0	Adrenalin intramuscularly.
Dilution in c.c.	3	5–9	7–9	8–11	
Trendelenburg.	0	0	0	0	Only if vasomotor collapse or if anesthesia too high.
Site of puncture.	L_5	L_3	L_3	L_2	
Stout.					
Dose in mgm.	100	150	150	200	Speed of injection. Perineum 5 seconds.
Ephedrine in mgm.	0	30	50	80	Lower abdomen 7 seconds.
Dilution in c.c.	1	1.5	2	2.5	Mid abdomen 10 seconds.
Trendelenburg.	0	0	0	0	Upper abdomen 12 seconds.
Site of puncture.	L_2–L_3	L_2–L_3	L_2–L_3	L_2–L_3	10 minutes after injection any position.
Rovenstine.					
Dose in mgm.	50–75 plus .5–.75 c.c. 10 per cent dextrose				
Ephedrine in mgm.	0				
Dilution in c.c.	1.5–2				For transurethral surgery, patient in lithotomy, head and shoulders elevated.
Trendelenburg.	0				
Site of puncture.	L_4–L_5				

Procaine. All solutions of procaine of anesthetic concentration are heavier than spinal fluid. Table IV is a summary of a few techniques with this agent by several workers.

Nupercaine. Crystals of nupercaine are neither soluble in spinal fluid nor in saline solution. Solutions of nupercaine as distributed are buffered solutions. The weaker solutions, 1:1000, 1:1500 and 1:2000, are acidified by the addition of a few drops of dilute hydrochloric acid. Of the techniques employing the 1:1500 solution it is felt by some that the Jones technique is safer than the Etherington-Wilson procedure. It is so considered because of the danger of too high an anesthesia following the injection of a light solution with the patient upright.

Romberger employs a combination of procaine and nupercaine thus employing a small volume, highly concentrated solution. The procaine in combination allows for a more rapid onset of anesthesia than if nupercaine were used alone. Table V lists techniques employing nupercaine.

Metycaine. The main advantage of metycaine over procaine lies in its slightly longer action. Many reports on this agent are as yet not available. The technique of Woodbridge is given in Table VI.

Pontocaine. Because the 1 per cent in saline solution of this agent for spinal anesthesia has a specific gravity close to

that of spinal fluid, adequate height of anesthesia is obtained best by the introduction of the drug at a higher level than with procaine. Because the agent is as apt to be slightly lighter as heavier than spinal fluid, the danger of a more complete anterior block with this agent than with heavier agents is feared. Fourteen cases of respiratory failure with this agent have recently been reported, with 2 resulting fatally.[4]

Bull and Esselstyn[4] feel that since this agent may be either lighter or heavier than the spinal fluid in a given case it is important to know exactly what their relationship is. They recommend the use of a solution of xylol and chlorobenzene with a gravity equal to that of pontocaine. Spinal fluid is not soluble in this solution and a drop added to it will either float or sink depending on its gravity.

TABLE V

NUPERCAINE TECHNIQUES

	Perineum	Lower Abdomen	Mid Abdomen	Upper Abdomen	Remarks
Keyes 1:200.					
Dose in mgm	10	10	10	10	
Ephedrine in mgm	100	100	100	100	
Dilution in c.c	2	5	8	10	
Trendelenburg	+	+	+	+	Immediate.
Site of puncture	L3	L3	L3	L3	Patient upright.
Jones 1:1500.					
Dose in mgm	4	6.6	8	10–12	
Ephedrine in mgm	60	70	80	90	Approximate.
Dilution in c.c	6	10	12	15–18	After injection patient prone 5 minutes.
Trendelenburg	+	+	+	+	
Site of puncture	L4	L1	L1	L1	Lateral position.
Wilson 1:1500.					
Dose in mgm	6.6	6.6	8	10	Patient upright.
Ephedrine in mgm	50	50	50	50	For low anesthesia 20 seconds.
Dilution in c.c	10	10	12	15	Mid anesthesia 30 seconds.
Trendelenburg	+	+	+	+	Upper anesthesia 40 seconds.
Site of puncture	L3	L3	L3	L3	
Romberger nupercaine-procaine combined.					
Dose in mgm. { Nupercaine	6–8	8–10–12			
Dose in mgm. { Procaine	75–100	120–240	...	.....	All abdominal cases blocked to nipple line.
Ephedrine in mgm	50	75			
Dilution in c.c	0.5–1	2–2.5			
Trendelenburg	+	+	...	.....	Delay, then use as needed.
Site of puncture	L4	L2–L1			

TABLE VI

METYCAINE TECHNIQUE

	Perineum	Lower Abdomen	Mid Abdomen	Upper Abdomen	Remarks
Woodbridge.					
Dose in mgm	40–80	120	140	180	Average.
Ephedrine in mgm	25	50	50	50	
Dilution in c.c	2	4–5	5	5	
Trendelenburg	0	Trendelenburg for height of anesthesia, then flat.			
Site of puncture	L4	L3	L3	L3	

A technique employing a pontocaine-glucose solution is advanced by Sise.[29] The addition of glucose increases the specific gravity, thus making the solution more controllable by changes in the tilt of the table. For perineal operations Sise recommends the addition of no glucose. I feel that following the introduction of a pontocaine-glucose solution through the fourth lumbar interspace using a small volume and with the head of the table elevated, a long lasting efficient anesthesia may be realized for perineal and transurethral surgery. In Table VII are listed the pontocaine techniques.

TABLE VII

PONTOCAINE TECHNIQUES

	Perineum	Lower Abdomen	Mid Abdomen	Upper Abdomen	Remarks
McCuskey.					
Dose in mgm	8	12	12	15	
Ephedrine in mgm	25	25	25	25	
Dilution in c.c	1.6	2.4	2.4	3	Approximate.
Trendelenburg	+	+	+	+	
Site of puncture	"One level higher than with procaine"				
Sise pontocaine-glucose.					
Dose in mgm	10–14	12–16	14–18	14–20	
Ephedrine in mgm	25	50	50	50	
Dilution in c.c	4–4.5	4–4.5	4–4.5	4–4.5	
Trendelenburg	10° for 1½ minutes, then flat				
Site of puncture	L3	L3	L3	L3	

Head and shoulders kept elevated by pillows.
For perineal operations no glucose with pontocaine.
For abdominal operations with patient flat equal parts pontocaine and 10 per cent glucose.
For abdominal operations with patient in Trendelenburg one-half as much glucose as pontocaine solution.

Pontocaine-glucose for perineal surgery.		
Dose in mgm	10–14	
Ephedrine in mgm	0–25	
Dilution in c.c	2–3	Equal volumes pontocaine and 10 per cent glucose.
Trendelenburg	0	Patient in lithotomy, head and shoulders elevated.
Site of puncture	L4–L5	Patient injected with head of table slightly elevated.

CARE OF PATIENT

Fall in Blood Pressure. Labat felt that a fall in blood pressure, even if great, would not result harmfully if cerebral anemia were prevented by the early use of the Trendelenburg position. It is CoTui's feeling that a systolic pressure of 70 mm. of mercury is at the critical level. He feels[8,9] that the Trendelenburg position in these patients is both useless and harmful. Most workers, however, do not hesitate to place their patients in this position provided sufficient time has elapsed after the injection of the drug to allow most of it to become fixed in nerve tissue. CoTui did not show that cerebral anemia is not prevented by this position in the presence of a low pressure. He succeeded in establishing that the head down position encouraged the flow cephalad of a highly concentrated solution of great gravity with resultant respiratory paralysis. CoTui showed also that the fall in blood pressure with its concommitant blood flow to tissues resulted in tissue anoxia.

Ephedrine, given to raise a fallen or rapidly falling pressure is probably best given by the method of Solkow as previously mentioned in this paper.

If the fall in pressure is due to loss of blood an immediate transfusion is indi-

cated. Fluid lost by perspiration is best replaced by a saline infusion. In the absence of loss of blood or other fluids from the blood stream there is some objection to the use of large volumes of fluid intravenously. A small volume of 50 per cent glucose intravenously might result beneficially although this requires some time to attract fluids back into the circulation and had best not be depended upon in an emergency. It finds its place in the immediate postoperative care.

Respiratory Depression or Paralysis. That the anterior roots are deliberately blocked to result in good surgical relaxation and that a high anterior block will result in a depression of respiration which might extend to a paralysis, are appreciated. It is because of this possible accident during spinal anesthesia that the anesthetist must be ever on the alert. For the first one-half hour of anesthesia he must determine every few minutes how high the motor paralysis has extended. The disappearance of thoracic respiration with an increasingly diaphragmatic type of breathing, loss of spoken voice, dilation of the alae nasi, the use of the accessory muscles of respiration with dropping of the jaw with each respiratory effort are signs of the presence of marked depression and on-coming paralysis. With the first sign of the onset of respiratory depression the patient should be exposed to high concentrations of oxygen. Even the administration of 100 per cent oxygen to a patient with extremely shallow respiration may not deliver sufficient oxygen to the alveoli to satisfy tissue needs. Pressure on the bag with each inspiration will help a good deal in carrying the oxygen further down the tracheobronchial tree. It is suggested that these patients be exposed to a mixture of helium oxygen (80–20 per cent respectively). The vehicle helium, being considerably lighter than nitrogen, makes this combination of gases more easily respirable. Muscles not paralyzed but weakened can thus carry in a stream of these gases much more readily than they can air. Carbon dioxide, though a definite respiratory stimulant, is felt by CoTui[10] to cause a further lowering of the blood pressure in patients under spinal anesthesia.

The presence of complete paralysis calls for artificial respiration either by chest compression or by rhythmic pressure on the rebreathing bag, filled with oxygen or helium oxygen. In the unconscious patient the introduction of an intratracheal tube will assure an open airway. The use of a Drinker respirator to maintain artificial respiration over a longer period of time may be employed.

Supplementary Anesthesia. Occurring more often with procaine than with pontocaine or nupercaine is the uncomfortable experience of having the operative procedure outlast the anesthesia. If the anesthesia begins to wane during abdominal closure the anesthetist may request the surgeon to infiltrate the recti with 1 per cent procaine to relieve muscular tension. With one hand under the peritoneum the solution is injected through a long needle carried through the exposed border of the rectus muscle deep into the muscle along its lateral borders. If the anesthesia begins to wear off during an upper abdominal operation, an anterior splanchnic block may be performed in addition.

To supplement a diminishing effect of the spinal anesthesia with either nitrous-oxide oxygen or ethylene oxygen is not satisfactory and has definite disadvantages. Sufficient relaxation is not obtained for upper abdominal closure nor for lower abdominal closure in vigorous patients. The patient under these gases is exposed to a minimum of oxygen. The latter is of definite danger since the patient may be just recovering from some degree of respiratory or circulatory depression with associated tissue anoxia. The only gaseous anesthetic which exposes the patient to a satisfactory amount of oxygen and which is capable of rendering sufficient relaxation in all but the most vigorous of patients is cyclopropane. This gas seems to be peculiarly adapted to this particular problem in

anesthesia. Patients insufficiently medicated or apprehensive can be kept asleep with a minimum of this gas even in the presence of good spinal anesthesia, with no harmful effects. In upper abdominal surgery the administration of this gas associated with spinal anesthesia abolishes the nausea, retching and vomiting that often occur. The oxygen content in the respired mixture may indeed render a useful purpose. It may to some degree abolish the tendency to tissue anoxia that might be present. Cyclopropane of itself can depress respiration. It is suggested that administration of this gas to a patient under spinal anesthesia be started with only partial carbon dioxide absorption. With the patient in Trendelenburg with viscera and packs interfering with the downward excursion of the diaphragm helium-oxygen with or without cyclopropane is sometimes of value in maintaining satisfactory pulmonary ventilation.

The administration of barbiturates intravenously has been recommended to supplement a waning spinal anesthesia. Inasmuch as the administration of a barbiturate by this method may be followed by a degree of respiratory depression and fall in blood pressure, there is much to say against this procedure particularly if the patient is recovering from just such a state of affairs.

COMPLICATIONS

In considering the relative postoperative morbidity following spinal and other methods of anesthesia a simple comparative percentage estimation is not sufficient to give a true estimate of their values. Of two series of cases it is likely true that spinal anesthesia was administered to many patients in whom an inhalation anesthesia was contraindicated. The presence of diabetes, nephritis and pulmonary complications may have placed these patients in the list of those having had spinal anesthesia. Patients in whom good relaxation was necessary for the surgery may have also been included. Patients in this latter group may have been suffering with intestinal obstruction, acute appendicitis with abscess formation, perforated duodenal ulcer and other upper abdominal surgery. All these are poor surgical risks and are the type of patients who develop postoperative complications. For that reason it is very difficult to determine exactly from published statistics the true relative dangers of the various types of anesthetic agents or procedures.

Emmett,[12] in a series of 1415 cases, employed this type of anesthesia five times as frequently as general anesthesia for biliary tract and stomach surgery. It was employed sixteen times for partial gastrectomy in comparison to general anesthesia which was employed but once. Of 5 deaths he attributes due to the anesthesia, 2 were respiratory and the remaining 3 he feels "might well be attributed to faulty selection of patients for spinal anesthesia." In spite of the much higher percentage of patients in whom upper abdominal surgery was done under spinal anesthesia and in spite of the fact also that almost twice as many intra-abdominal operations were performed under this method, the incidence of violent respiratory infections under this procedure was exactly the same as that occurring after 1541 cases of general anesthesia. Of 526 intra-abdominal cases operated upon under general anesthesia 4 developed violent respiratory infections, an incidence of 0.76 per cent. Of 1013 spinal anesthesias for intra-abdominal surgery the postoperative incidence of violent respiratory complications was 5, or 0.49 per cent. Mild respiratory infections, however, were greater following spinal anesthesia. In these series of cases no death occurred from spinal anesthesia in a patient who was a good surgical risk.

Hanisch[13] comparing the postoperative complications in 150 cases done under spinal anesthesia with a like number done under ether finds the pulmonary complications about equal in both groups. King[15] reporting 1500 cases of spinal anesthesia finds no death due directly to the anesthesia. The anesthesia may have perhaps

acted as a contributory factor in 6 deaths, he feels. The operative findings in these 6 cases are: (1) intestinal obstruction with gangrene of ileum; (2) multiple penetrating and perforating gunshot wounds of the abdomen; (3) acute intestinal obstruction; (4) strangulated inguinal hernia with perforation of the sigmoid and generalized peritonitis; (5) strangulated femoral hernia and (6) hypertrophied prostate. Pulmonary complications were manifest in 6.8 per cent of these patients. This includes all types of respiratory involvement and is felt by King to be low.

Orkin,[25] in studying collected statistics from many clinics, finds that the incidence of postoperative pulmonary complications is high. Rapoport[26] investigated the comparative postoperative morbidity following the use of both spinal and inhalation anesthesia for five different types of surgical procedures. The totals in each series were fairly close. The percentage incidence for all complications, pulmonary complications and deaths were all lower in the spinal anesthesia series. Here, again, complications were less despite the fact that in these series there were more than two and one-half times as many upper abdominal surgical procedures done by this method as were done under general anesthesia.

The annual report of the Waters group at Madison, for the year 1935, as well as for the two previous years, presents a complete and painstaking analysis of the relationship of postoperative complications to anesthetic agents and methods. Major respiratory complications following all types of anesthesia occurred in 1.58 per cent of the cases. The incidence of the same type of complication following ether anesthesia was 3.13 per cent and after spinal anesthesia it was 1.17 per cent.

INDICATIONS AND CONTRAINDICATIONS

Spinal anesthesia may be employed for any operation below the diaphragm. This procedure has been recommended for thoracic surgery. With our present techniques an anesthesia for thoracic surgery calls for higher punctures, greater dosage or both. Inasmuch as attempts to produce as high an anesthesia as is necessary for this type of surgery increase the concentration of the agent higher up in the canal than is usual for intra-abdominal surgery, a more thorough interference with respiration may result. Thus, the chances for respiratory failure are greater. Thoracic surgery may easily be done under the gases with cyclopropane particularly suited.

Spinal anesthesia is indicated in the presence of pulmonary disease as bronchitis, brochiectasis, emphysema, active tuberculosis and asthma. Since this procedure has less effect on blood sugar than does ether anesthesia it is indicated in the presence of diabetes. Since it seems to have less irritant effect on the kidneys renal disease may indicate its use. Patients suffering from advanced surgical shock, hemorrhage or marked debility do not stand the procedure very well and contraindicate its use. Patients with extremes in blood pressure also do not do well under this method. The presence of skin infection at the puncture site or cerebrospinal syphilis contraindicate the method.

Simple superficial surgical procedures had best be done under some other method of regional or inhalation anesthesia. In operations of the lower extremities where a good deal of relaxation is desired, as in open reduction of the femur, this method is of value.

It seems to be the anesthesia of choice in transurethral surgery, strangulated hernias, and acute intra-abdominal surgery, with the exception of ruptured tubal pregnancy and hemorrhage. Intra-abdominal surgery requiring adequate exposure and relaxation in vigorous and muscular adults is aided by this method.

Patients with acute intestinal obstruction in whom an attempt is to be made to relieve the cause of the obstruction, as freeing of adhesions, are benefited by spinal anesthesia. In advanced cases of obstruction in whom only relief from the toxemia

is to be attempted as colostomy or ileostomy, simple field block may be sufficient.

CONCLUSIONS

The administration of spinal anesthesia is technically simple. The ability to perform a lumbar puncture and inject an anesthetic solution does not qualify one to administer a spinal anesthesia to a human being. A knowledge of the fundamentals, agents and methods of spinal anesthesia coupled with proper and intelligent choice and care of patients will do much to diminish the number and severity of accidents attributable to this method of anesthesia.

REFERENCES

1. Anderson, E. L.: Case of trophoneurotic gangrene of extremity following spinal anesthesia. *Journal-Lancet*, 55: 800 (Dec. 15) 1935.
2. Balyeat, R. M. and Rinkel, H. J.: Urinary retention due to the use of ephedrine. *J. A. M. A.*, 98: 1545 (Apr. 30) 1932.
3. Brock, S., Bell, A. and Davison, C. Nervous complications following spinal anesthesia. *J. A. M. A.*, 106: 441 (Feb. 8) 1936.
4. Bull, D. C. and Esselstyn, C. B. Pontocaine in spinal anesthesia. *Ann. Surg.*, 103: 29 (Jan.) 1936.
5. Chen, K. K., and Schmidt, C. F. The action and clinical use of ephedrine. *J. A. M. A.*, 87: 836 (Sept. 11) 1926.
6. Colwell, A. R. Suppression of glucose combustion by epinephrine administration. *Endocrinology*, 15: 25 (Jan.-Feb.) 1931.
7. CoTui, F. W. Effect of different narcotics and narcotic combinations on minimum lethal dose of procaine hydrochloride intracisternally. *Jour. Pharmacol. and Exper. Therap.*, 48: 229 (June) 1933.
8. *Ibid.* Further studies in subarachnoid anesthesia. *Anesth. and Analg.*, 13: 183 (Sept.-Oct.) 1934.
9. *Ibid.* Further studies in subarachnoid anesthesia. *Anesth. and Analg.*, 13: 143 (July-Aug.) 1934.
10. *Ibid.* Spinal anesthesia: the experimental basis of some clinical practices. To be published.
11. Davis, L., Haven, H., Givens, J. H. and Emmet, J. Effects of spinal anesthetics on spinal cord and its membranes; experimental study. *J. A. M. A.*, 97: 1781 (Dec. 12) 1931.
12. Emmett, J. M. Spinal anesthesia; 1415 cases of, with especial reference to indications, complications and mortality. *Virginia Med. Month.*, 62: 304 (Sept.) 1935.
13. Hanisch, L. E. Ether and spinal anesthesia, a comparative study of complications in. *Nebraska State Med. Jour.*, 18: 298, 1933.
14. Jones, W. H. Percain: a new regional and spinal analgesic, with special reference to high thoracic nerve root block and new technique. *Anesth. and Analg.*, 9: 218 (Sept.-Oct.) 1930.
15. King, O. C. Spinal analgesia: a report of 1500 cases. *Ann. Surg.*, 101: 690 (Feb.) 1935.
16. Koster, H. and Kasman, L. P. Histologic studies of spinal cord following spinal anesthesia. *Am. Jour. Surg.*, 25: 277 (Aug.) 1934.
17. Lindemulder, F. G. Spinal anesthesia: its effect on the central nervous system. *J. A. M. A.*, 99: 210 (July 16) 1932.
18. Lundy, J. S. Outline of some of the advantages and disadvantages of various agents used in anesthesia. *Minn. Med.*, 15: 219 (April) 1932.
19. *Ibid.* Advances in anesthesia from the standpoint of the anesthetist. *J. A. M. A.*, 99: 968 (Sept. 17) 1932.
20. Lundy, J. S., Essex, H. E. and Kernohan, J. W. Experiments with anesthetics. IV. Lesions produced in the spinal cord of dogs by a dose of procaine hydrochloride sufficient to cause permanent and fatal paralysis. *J. A. M. A.*, 101: 1546 (Nov. 11) 1933.
21. Lundy, J. S., Essex, H. E. and Kernohan, J. W. Experiments with anesthetics; lesions of spinal cord in dogs produced by dose of procaine sufficient to cause permanent and fatal paralysis. *Proc. Staff Meet. Mayo Clin.*, 8: 88 (Feb. 8) 1933.
22. Marvin, F. W. Present status of various spinal anesthetics and their clinical usefulness. *J. A. M. A.*, 101: 1475 (Nov. 4) 1933.
23. Meek, W. J. and Seevers, M. H. Cardiac irregularities produced by ephedrine and protective action of sodium barbital. *Jour. Pharm. and Exper. Therap.*, 51: 287 (July) 1934.
24. Nonne, M. and Demme, H. Degenerative Myelitis nach Spinal-Anasthesie. *Wien. klin. Wchnschr.*, 41: 1002 (July) 1928.
25. Orkin, L. D. Reported mortality and morbidity following spinal anesthesia. *Tr. Am. Soc. Reg. Anesth.* p. 1 (Mar. 3) 1936.
26. Rapoport, B. A comparison of postoperative complications following general and spinal anesthesia. *New Eng. Jour. Med.*, 213: 1235 (Dec. 19) 1935.
27. Saklad, M. Spinal anesthesia: agents, methods and indications. *New Eng. Jour. Med.*, 213: 1226 (Dec. 19) 1935.
28. Seevers, M. H. and Meek, W. J. The cardiac irregularities produced by ephedrine after digitalis. *Jour. Pharmacol. and Exper. Therap.*, 53: 295 (Mar.) 1935.
29. Sise, L. F. Pontocaine-glucose solution for spinal anesthesia. *S. Clin. North America*, 15: 1501 (Dec.) 1935.
30. Solkow, M. L. Intravenous infusion of ephedrine in saline in spinal anesthesia. *Tr. Am. Soc. Reg. Anesth.* p. 22 (May 5) 1936.
31. Stein, J. J. and Tovell, R. M. Spinal anesthesia. *Amer. Jour. Surg.*, 30: 282, 1935.
32. Valentine, J. J. and Fitzgerald, J. S. Retention of urine due to ephedrine with discussion of mode of action. *Jour. Urol.*, 34: 314 (Oct.) 1935.
33. Wiedhopf, O. Pantokain, ein neues Lokalanasthetikum. *Deutsche med. Wchnschr.*, 57: 13 (Jan. 2) 1931.

REGIONAL ANESTHESIA FOR OPERATIONS ON THE NECK

RALPH M. TOVELL, M.D.*

Section on Anesthesia, The Mayo Clinic

ROCHESTER, MINNESOTA

CHOICE of anesthesia for operations on the neck frequently proves difficult. For many operative procedures, inhalation anesthesia is satisfactory to both patient and surgeon, but in certain instances inhalation anesthesia may present difficulties unless an intratracheal tube is used. General anesthesia produced by pentothal sodium solution injected intravenously is satisfactory for operative procedures of short duration. Regional anesthesia, however, has a definite field of usefulness if patients are suffering from asthma, bronchitis, emphysema, bronchiectasis, or other conditions that contraindicate the use of general anesthesia. For certain operative procedures, particularly those involving the larynx, it is essential that the cough reflex be maintained throughout; regional anesthesia will permit this. Patients suffering from carcinoma of the tongue may require ligation of the external carotid artery preliminary to fulguration of the lesion. Paravertebral block will provide adequate anesthesia for this operation and the danger of postoperative pneumonia is reduced to a minimum. Reference to further application of regional methods will be made later in this article.

ANATOMY

The sensory innervation of the neck is chiefly through the second, third and fourth cervical nerves (Fig. 1). After emerging from their respective intervertebral foramen, each of these nerves passes behind the vertebral artery and reaches the tip of the corresponding transverse process at which point they become accessible for blocking by the paravertebral method, either by the lateral or posterior routes. Paravertebral block or deep cervical block is the term applied to a method by which anesthesia is produced by distributing an anesthetic drug in solution close to the vertebral column in the region where the

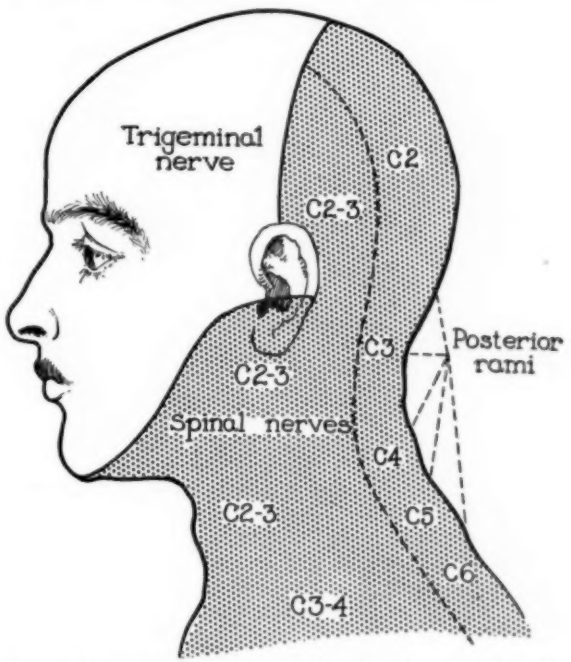


FIG. 1. Sensory innervation of head and neck. (Tovell. *Surg. Clin. N. Amer.*, 15: 1277–1292 [Oct.] 1936.)

nerves emerge from the intervertebral foramina. To reach these points, needles may be inserted through the structures of the neck lying lateral to the transverse process, or through those lying posterior to the transverse processes. The lateral route is employed when the operative procedure is to involve anterior or lateral structures of the neck and the posterior route is employed for operations such as insertion of a bone graft or laminectomy.

The posterior primary divisions of the cervical nerves supply the posterior structures of the neck and head, and overlap, in the upper region of the back, the area supplied by the dorsal nerves. The anterior primary division of the second, of the third, and of the fourth cervical nerves each

* After Sept. 1, 1936, Chief Anesthetist, Hartford Hospital, Hartford, Conn.

divides into an ascending and descending branch. These branches are connected in a series of loops which lie close to the transverse cervical processes, under cover of the sternocleidomastoid muscle, thus they constitute the cervical plexus (Fig. 2). From these loops, superficial and deep branches are given off. The superficial cervical branches pierce the deep fascia of the neck at a point midway between the origin and the point of insertion of the sternocleidomastoid muscle (Fig. 3). From this point the lesser occipital, great auricular, cutaneous colli, and the three supraclavicular nerves radiate to supply their respective cutaneous regions. These nerves may be blocked as they emerge from the deep fascia (superficial cervical block), or the cutaneous areas which they supply may be infiltrated.

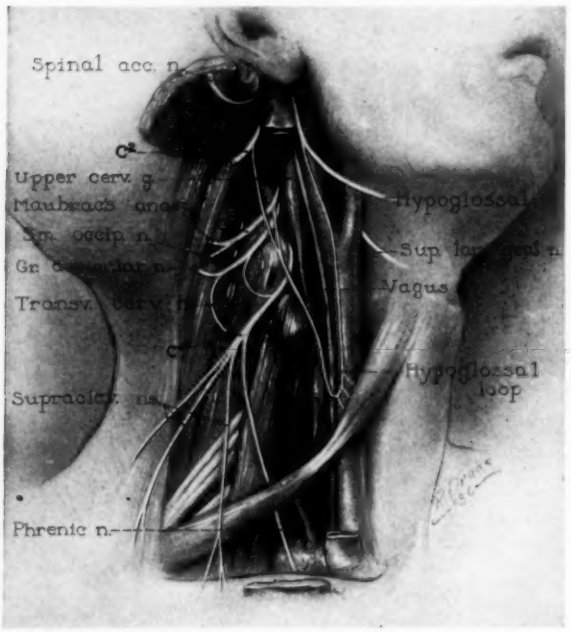


Fig. 2. The anterior primary divisions of the second, third and fourth cervical nerves enter into the formation of the cervical plexus (semidiagrammatic). The ansa hypoglossal nerve which supplies the muscle overlying the thyroid gland may be noted.

Fig. 3. Superficial branches of the cervical plexus and the areas which they supply. (Tovell. *Surg. Clin. N. Amer.*, 15: 1277–1292 [Oct.] 1936.)

PRELIMINARY MEDICATION

If regional anesthesia is to be successful, preliminary medication must be adequate to allay fear, and thus retard the production of excessive amounts of epinephrine. It is also essential to provide prophylaxis against any untoward reaction to procaine. Sodium ethyl 1-methylbutyl barbituric acid (pentobarbital sodium) grains 1.5 (0.097 gm.) or grains 3 (0.20 gm.), may be given orally an hour before bedtime the night prior to operation. Another dose of 1.5 grains of the same sedative may be administered orally at 7 o'clock on the morning of operation. An hour before operation the patient may be given 1.5 or 3 grains of pentobarbital sodium orally. Morphine, grain $\frac{1}{6}$ (0.01 gm.) with atropine, grain $\frac{1}{150}$ (0.0004 gm.) may be given by hypodermic injection at the same time. Decision regarding the amount of pentobarbital sodium may be based on the patient's response to the dose administered the night previous to operation.

CERVICAL BLOCK: POSTERIOR ROUTE

The patient lies face downward. His thorax is supported on pillows, and his head is bent forward until his forehead touches the table. The spinous processes can be defined by palpation and counted from the seventh, which is most prominent. The sixth cervical vertebra has the most prominent transverse process (tubercle of Chassaignac), and this is on a level with the cricoid cartilage. A wheal is raised 2 cm.

lateral to the median line on each side (Fig. 4) opposite the spinous process of the second cervical vertebra. Intracutaneous injection is continued from these points as far as it may be necessary to block. This procedure is less painful than is that of raising individual wheals for insertion of each needle. An 80 mm. needle is introduced through the wheal first raised; it is inserted laterally and anteriorly until the point impinges on the posterolateral aspect of the transverse process of the vertebra. The needle is then partially withdrawn and reintroduced in a slightly more oblique direction. It is inserted 1 cm. beyond the point at which the bone of the lateral aspect of the vertebral arch (Fig. 5) was last palpated and 5 c.c. of a 1 per cent solution of procaine (Fig. 6) with cobefrin (Fig. 7), is injected. This solution should be warm. Preliminary aspiration is always made to prove to the anesthetist's satisfaction that the needle has not entered a vessel and that the injection will not be intravascular. The entire procedure is then repeated on the opposite side. When all the needles are

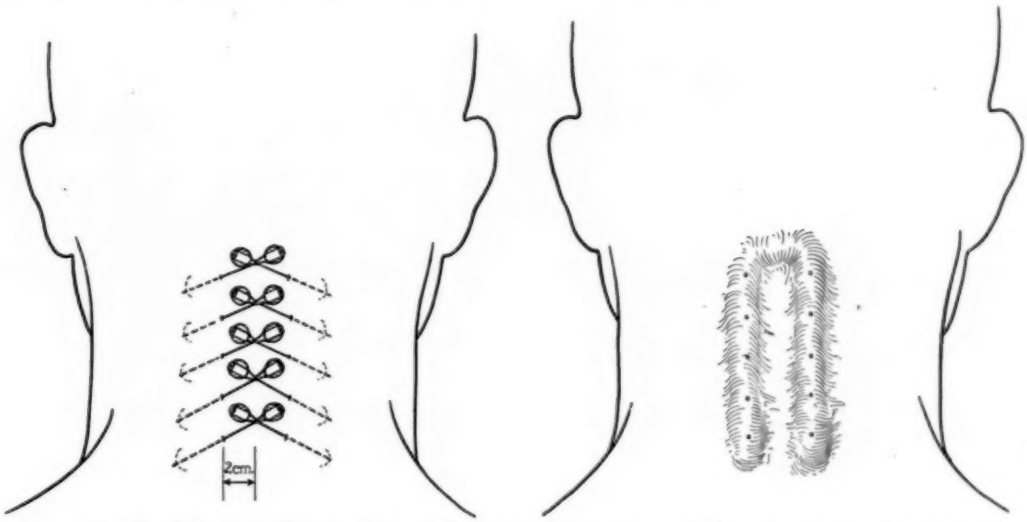


Fig. 4. Cervical block by the posterior route; 5 c.c. of 1 per cent solution of procaine with cobefrin is injected through each needle. Infiltration with a solution of 0.5 per cent procaine with cobefrin intradermally and subcutaneously in the shape of an inverted U completes the block.

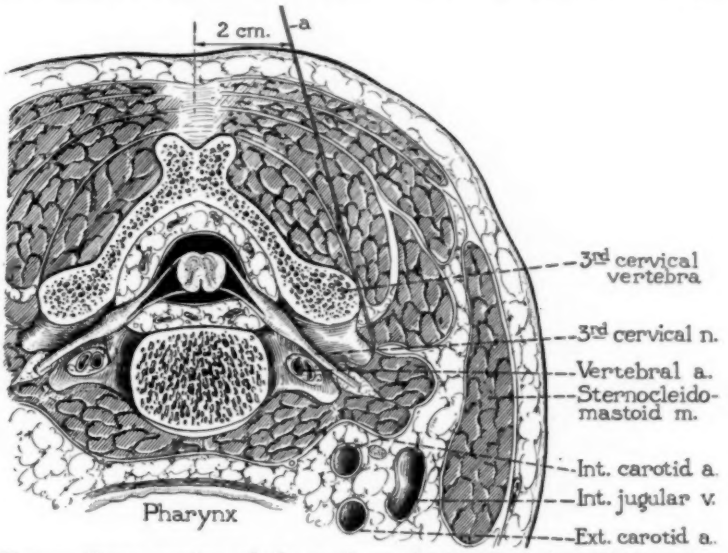


Fig. 5. Cross section of the neck at the level of the third cervical vertebra, indicating the line of insertion the needle must follow when deep cervical block is undertaken by the posterior route.

similarly placed, one is confronted with two lines of needles, the shafts of which cross the median line. Following injection, the needles are withdrawn and the space between each two points of insertion is infiltrated (Fig. 4) with a cold 0.5 per cent solution of procaine with cobefrin. The injection is made both intradermally and subcutaneously, and is carried down to the level of the transverse processes. A similar injection is made across the median line between the first two wheals raised on each side, opposite the spine of the second cervical vertebra, thus completing the block.

When the infiltration is made with a cold solution, the duration of anesthesia will be sufficient for exploratory laminectomy or for insertion of a bone graft. This method is particularly useful for insertion of a bone graft when the general condition of the patient contraindicates the use of inhalation anesthesia. In order to obtain the graft, the area of the tibia required may be rendered insensitive by field block anesthesia.[1] A solution of 0.5 per cent procaine with cobefrin will produce the desired result. Laminectomy performed to relieve pressure on the spinal cord may be accomplished without supplementary anesthesia. In the course of the removal of a tumor of the spinal cord, if it is necessary to interfere with a posterior nerve root, the patient will complain of pain, and supplementary general anesthesia may be required temporarily during this phase of the operation.

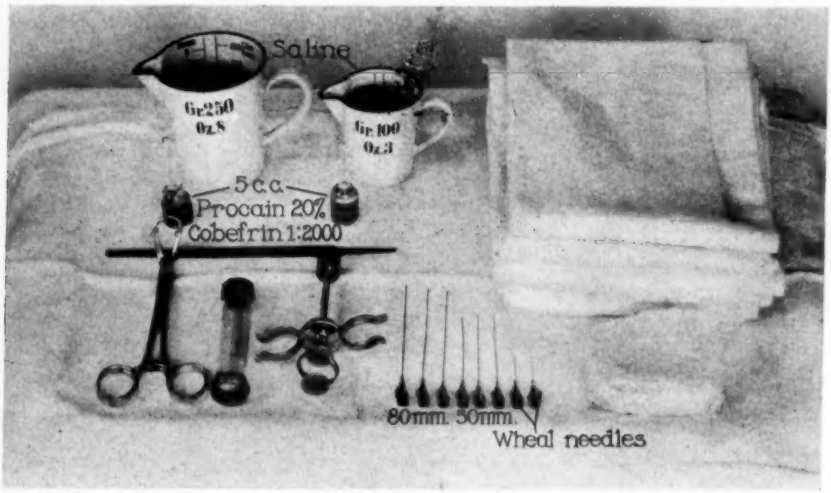
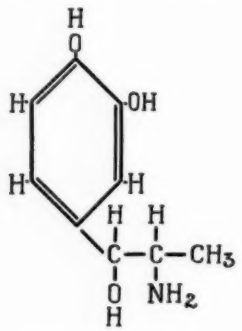


Fig. 6. Tray for regional anesthesia. The contents of one ampoule are added to the 95 c.c. of saline solution in the small graduate to make a 1 per cent solution of procaine and cobefrin 1:40,000. The contents of the second ampoule, added to the 195 c.c. of saline solution in the large graduate, make a 0.5 per cent solution of procaine and cobefrin, 1:80,000.



Cobefrin

Fig. 7. Cobefrin (1, 2-dihydroxyphenyl-4-propanolamine) is a vasoconstrictor similar in action to epinephrine except that it is less likely to cause pallor, palpitation, or syncope in comparative dosages.

DEEP CERVICAL BLOCK: LATERAL ROUTE

The patient lies on his back, with his head, supported by one thin pillow, turned well toward the side. The tip of the mastoid process is palpated. A wheal, raised 1 cm. posterior and 1 cm. caudad to the tip,

[1] Lundy, J. S. and Tovell, R. M. The technique of nerve blocking for various orthopaedic operations. *Brit. Jour. Anaestbesia*, 12: 52–61 (Jan.) 1935.

indicates the point of insertion for the 80 mm. needle by means of which the second cervical nerve may be blocked. Next, the external jugular vein is compressed at a point immediately above the clavicle. The vein becomes distended and the point at which it crosses the posterior border of the sternocleidomastoid muscle is readily noted. Another wheal is raised 1 cm. posterior and 1 cm. cephalad to this point. A needle 50 mm. in length used in blocking the fourth cervical nerve is inserted through the lower wheal. In order to block the third cervical nerve, a similar needle is inserted through a wheal raised midway between the two (Fig. 8).

A right-handed anesthetist stands at the head of the operating table when injecting the anesthetic into the patient's right side, and when injecting into the left side, he finds it convenient to stand facing the patient's left side. For a left-handed anesthetist the stance is reversed. An 80 mm. needle is inserted through the upper wheal, and the forefinger of the other hand is used to palpate the tip of the prominent transverse process of the sixth cervical vertebra. The needle is directed downward, inward and backward until bone is encountered. It is essential that the needle impinge upon the most superficial bone in the region (Fig. 9). In order to accomplish this the needle should not be inserted directly inward because of the likelihood of missing the tip of the transverse process and of entering the spinal canal instead. It is an aid if the needle is guided in the direction of the finger which is palpating the tip of the transverse process of the sixth cervical vertebra. Fifty mm. needles are inserted through the second and third wheals in a similar manner. Through each of the three needles 10 c.c. of 1 per cent solution of procaine with cobefrin is injected in divided doses, after it has been demonstrated by aspiration that each needle is neither within a blood vessel nor within the dura. This is the basic procedure employed to establish regional anesthesia for operations involving lateral and anterior structures of the neck.

SUPERFICIAL CERVICAL BLOCK

Superficial cervical block constitutes the second line of defense in providing anesthesia for a major surgical operation on the neck. The superficial branches of the cervical plexus may be blocked as they wind over the posterior border of the sternocleidomastoid muscle; 20 c.c. of a 0.5 per cent solution of procaine with cobefrin may be used, and should be injected subcutaneously over the sternocleidomastoid muscle (Fig. 10).

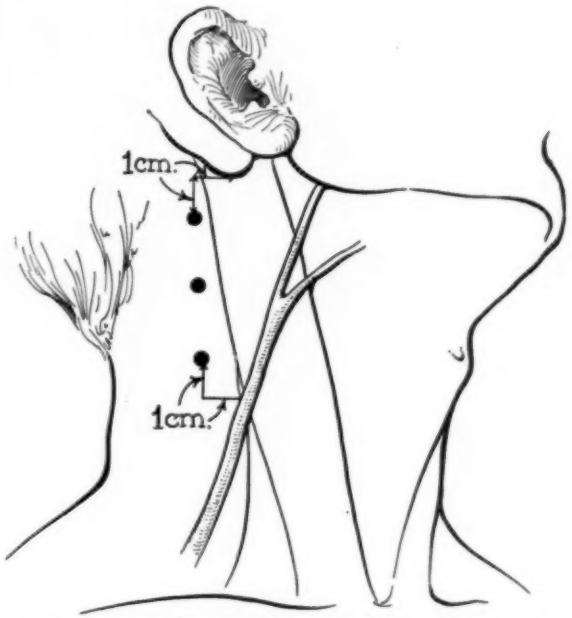


Fig. 8. Landmarks for deep cervical block. The upper wheal through which the second cervical nerve is reached is raised 1 cm. posterior and caudad to the tip of the mastoid process. The lower wheal through which the fourth cervical nerve is reached, is raised 1 cm. posterior and cephalad to a point at which the external jugular vein crosses the posterior border of the sternocleidomastoid muscle. The wheal for the third cervical nerve is raised midway between these two.

For operations necessitating an incision in the midline posteriorly, cervical block by the posterior route followed by infiltration as described in the foregoing, is sufficient. For major operations which involve the anterolateral structures of the neck, deep cervical block by the lateral route followed by superficial cervical block, are the basic procedures required to produce regional anesthesia. Additional procedures must be undertaken for certain operations,

and for all operations it is customary to establish a third line of defense by infiltrating intracutaneously in the line of incision.

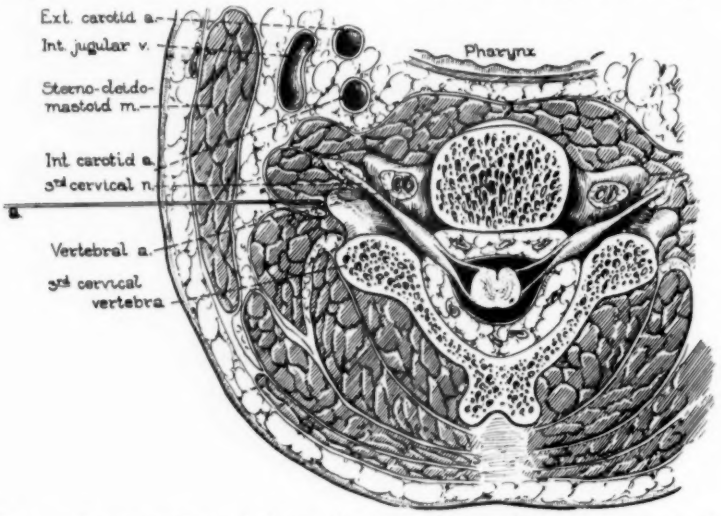


Fig. 9. Cross section of the neck at the level of the third cervical vertebra, indicating the line of insertion the needle must follow when deep cervical block is undertaken by the lateral route. (Tovell. *Surg. Clin. N. Amer.*, 15: 1277–1292 [Oct.] 1936.)

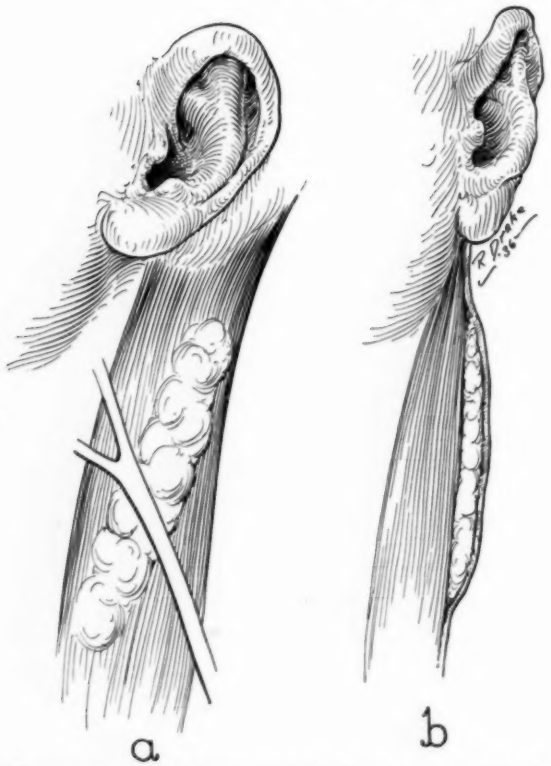


Fig. 10. Superficial cervical block is accomplished by injecting subcutaneously 20 c.c. of 0.5 per cent solution of procaine with cobefrin (*a*) deep to the external jugular vein but (*b*) over the sternocleidomastoid muscle.

SUPERIOR LARYNGEAL BLOCK

For laryngofissure, or laryngectomy, it is necessary to block the superior laryngeal nerves on each side. The interval between the hyoid bone and the thyroid cartilage is located (Fig. 11). A 50 mm. needle may be introduced through the skin overlying the depression between these two structures, and inserted inward and posteriorly until the first sense of resistance has been passed; 5 c.c. of a 1 per cent solution of procaine with cobefrin is injected slowly, and the procedure is repeated on the opposite side. This injection may be made without danger, provided tracheotomy has been performed. If a tracheal stoma is not present, the point of the needle may reach to the submucosa layer. Injection in this situation may produce an edematous bleb within the larynx, and a partial obstruction may thus be converted into a complete obstruction. If during the injection the patient complains of his breathing, or if he coughs, it is well to discontinue injection temporarily. The needle should be partially withdrawn before the injection is completed.

To complete the block for laryngectomy, and to provide anesthesia of sufficient duration, it is well to infiltrate the skin bilaterally with a cold solution of 0.5 per cent procaine with cobefrin along the lines *a* to *b* to *c* to *d* (Fig. 12). Following this type of preparation the vocal cords may be exposed or the larynx may be removed without causing undue pain. It will be necessary

for the surgeon to infiltrate the tissue between the larynx and esophagus in order to desensitize twigs from the vagus nerves. An injection of 10 c.c. of 0.5 per cent solution of procaine with cobefrin on each side will usually suffice for this purpose. With the same preparation, bilateral deep and superficial cervical block followed by infiltration, as indicated in Figure 12, may be employed preliminary to excision of a cyst of the thyroglossal duct, provided the injections are carried deep enough to desensitize the base of the tongue. Unilateral deep block and superficial cervical block have been found particularly useful as a preparation for ligation of an external carotid artery or for the first stage of excision of a diverticulum of the esophagus. For the second stage, infiltration on each side of the line of incision is sufficient. When the submental and submaxillary glands are to be removed it is necessary to employ the basic anesthetic procedures and also to infiltrate 0.5 per cent solution of procaine with cobefrin along the line of the jaws and the line of the incision (Fig. 13). It is also essential that the floor of the mouth be injected in several places, 5 c.c. of a 0.5 per cent solution of the same anesthetic being deposited in several regions as indicated in Figure 13. For excision of cervical lymph nodes for biopsy, anesthesia may be produced by means of a field block, that is, infiltration around and under the lesion. For tracheotomy or for interruption of the phrenic nerve, infiltration in the line of incision has proved satisfactory.

Fig. 11. Blocking the superior laryngeal nerve.

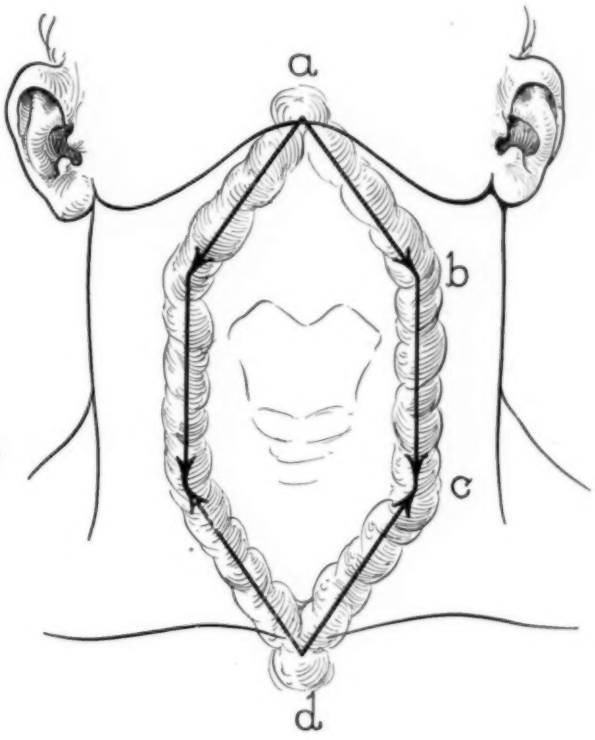


Fig. 12. Lines of intradermal and subcutaneous injection in final preparation for an incision in the median line.

For operations on the thyroid gland, the basic anesthetic procedures, deep and superficial cervical block,[2] may be employed. In the majority of cases, however, satisfactory anesthesia may be produced by superficial cervical block followed by infiltration of the skin and subcutaneous tissue in the line of incision and in the region of the flap that is to be raised. An injection of 10 c.c. of a 1 per cent solution of procaine with cobefrin (Fig. 14, *a-b*) is

[2] Lundy, J. S. Local anesthesia for operations on the neck. *Current Res. Anesth. and Analg.*, 8: 153–160 (May-June) 1929.

usually sufficient to accomplish superficial cervical block on each side. From 60 to 80 c.c. of a 0.5 per cent solution of procaine

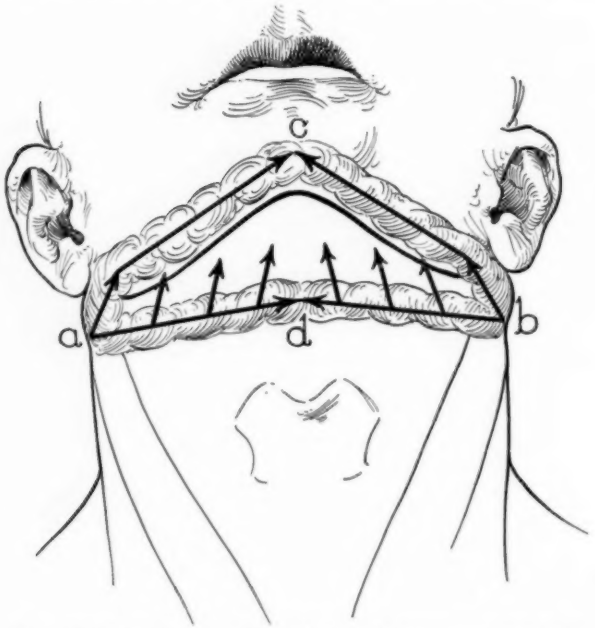


FIG. 13. For certain operations it is necessary to infiltrate intradermally *a* to *c* to *b* over the lower margin of the jaws. The line of incision *a* to *d* to *b* is also infiltrated with 0.5 per cent solution of procaine with cobefrin. From this line the floor of the mouth may be injected in several places, as indicated by the arrows.

with cobefrin is usually sufficient for the infiltrative part of the procedure (Fig. 14, *a-c*, *a-d*, *a-e*). The descendens hypoglossi,[3] the nerves supplying the sternohyoid and sternothyroid muscles, may be blocked by injecting subcutaneously 5 c.c. of a 1 per cent solution of procaine with cobefrin immediately anterior to the anterior border of each sternocleidomastoid muscle on a line (Fig. 14, *f*) between the notch of the thyroid cartilage and the point at which the external jugular vein crosses the posterior border of the sternocleidomastoid muscle. Following this type of injection it may be necessary for the surgeon to infiltrate the region of the superior pole of the thyroid gland as it is approached. The alternative method is to administer "gas" to the patient during the short interval of

[3] BARTLETT, WILLARD and BARTLETT, WILLARD, JR. A safe and satisfactory method of anaesthesia for toxic goiter patients. *Surg., Gynec., and Obst.*, 58: 737–740 (April) 1934.

intervention in this region. Nitrous oxide may be used for this purpose, but for a patient with a high basal metabolic rate,

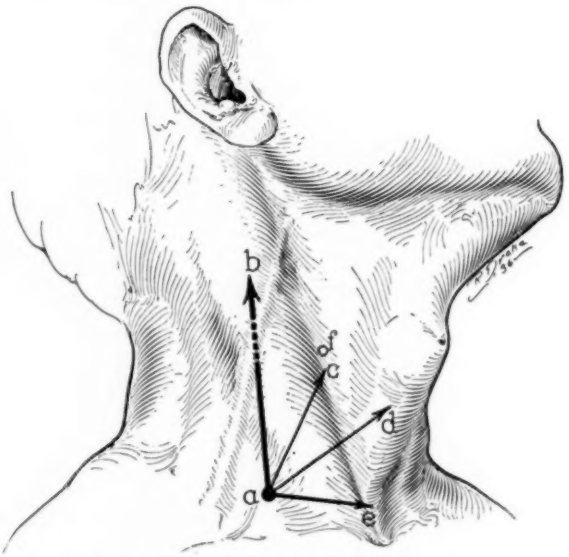


FIG. 14. Superficial vertical block (*a-b*) may be produced by infiltrating subcutaneously over the sternocleidomastoid muscle on each side with 10 c.c. of 1 per cent procaine and cobefrin 1:40,000. The descending hypoglossal nerve and the descending cervical nerve may be blocked on each side with 5 c.c. of 1 per cent procaine and cobefrin solution at a point (*f*) immediately anterior to the sternocleidomastoid muscle, on a line between the notch of the thyroid cartilage and the point at which the external jugular vein crosses the posterior border of the sternocleidomastoid muscle. Infiltration (*a-c*, *a-d*, *a-e*) with 0.5 per cent procaine and cobefrin solution completes the block.

for whom the need for oxygen is increased over the normal, cyclopropane is an extremely useful gas. With this potent gas, adequate anesthesia may be maintained without the production of anoxemia.

For patients with gross distortion of the neck caused by multiple large adenomas, resort to combined bilateral deep and superficial cervical block is good practice. A procedure dependent on bony landmarks is preferable to one dependent on landmarks in soft tissue that has become distorted. Inhalation anesthesia may be used to supplement the regional anesthesia in the few cases in which it is necessary, and if signs of obstruction should develop, an intratracheal tube may be introduced. A detailed consideration of that problem does not come within the scope of this paper.

CAUDAL AND TRANSSACRAL BLOCK

BRIAN C. SWORD, M.D.

Attending Anesthetist, Grace Hospital and Chairman of the Department of Anesthesia

NEW HAVEN, CONN.

FOR the past three decades or more it has been known that any of the desired spinal nerves may be blocked for anesthetic purposes. The term caudal transsacral block was first employed by the late Gaston Labat, and it is one of our most dependable forms of regional anesthesia in selected cases.[1] In 1935 Lundy subdivided caudal block into high and low. Caudal block is performed by depositing the anesthetic solution through the sacral hiatus into the caudal canal, while transsacral block is accomplished by injecting the sacral foramina on either side. While this procedure has been described very clearly by Labat and others, the technique followed in this hospital has been the one described by Lundy.

The patient is placed in the prone position with the hips elevated about 7.5 cm. by a pillow or other means, carefully prepared surgically using metaphen, and then draped with sterile towels and sheets.

In order to find the point at which the caudal needle should enter the skin,[2] a right-handed anesthetist ought to stand at the left of the operating table and places the tip of his left index finger over the distal end of the coccyx. The tip of the thumb, when it is held in a vertical position, will rest in a small triangular shaped depression over the sacrum, which is bounded above by a horizontal line drawn from one sacral cornu to the other, and may be completed by lines converging downward from either cornu to a protuberance in the median line that represents the distal end of the sacrum. The intradermal wheal, through which the caudal needle must pass, should be raised in the center of this triangle.

The wheal is then immobilized by pressure with the left index finger. A medium caliber needle, 50 mm. long is attached to the spring and inserted through the wheal, and directed through the sacrococcygeal membrane into the caudal end of the sacral canal, slowly injecting 5 c.c., of a 1 per cent solution of procaine. The syringe is detached but the needle should be left in situ as a guide for the introduction of the caudal needle.

Insertion of caudal needle, as outlined by Lundy, is as follows: The caudal needle is grasped between the thumb and middle finger of the right hand, the index finger pressing the stilet into the needle. The left index finger is again returned to the median line and the tissue is immobilized as in Figure 1. The 50 mm. needle is grasped between the ring and little fingers and withdrawn and dropped, but one must not glance away from the primary wheal. The caudal needle is thrust through the perforation made by the 50 mm. needle and advanced through the sacrococcygeal membrane until bone is reached. It is then rotated by the thumb and middle finger, the index finger holding the point gently against bone. After the bevel has thus been brought against the bone, the hilt of the needle is depressed and the shaft advanced through the sacrococcygeal membrane into the caudal canal.

When bony resistance is encountered at points low in the caudal canal the caudal needle is given a half turn (180°) and again advanced. The object of rotating the needle is to bring its bevel against the bony obstruction so that the needle will override it. With the left index finger one may massage the soft tissues overlying the sacrum and frequently facilitate the upward movement of the caudal needle when it apparently becomes lodged in the sacral canal. It is especially advantageous to press the tip of the left index finger into the fossa between the sacral cornua in order to depress the point of the caudal needle and force it into the sacral hiatus. The caudal needle is advanced into the caudal canal until its point comes to rest at the level of the third sacral foramen.

It is desirable that the point of the needle be brought as nearly as possible into the center of the caudal canal, that is, in the

center of all its diameters. One may estimate how high the point of the needle lies in the canal by measuring the stilet of the

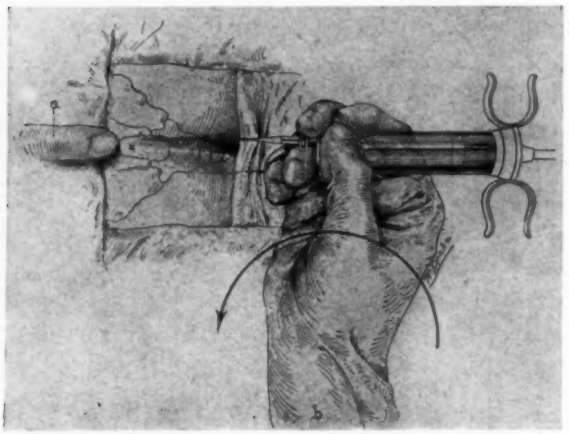


Fig. 1. Introduction of the 50 mm. needle; *a*, the left index finger; *b*, the right hand holding syringe and 50 mm. needle; *x*, the spot through which the needle is to be thrust. (Tovell, R. M. in Curtis, Gynecology and Obstetrics, Vol. 3. Saunders Co., 1933.)

needle against the skin posterior to the sacral spines. If the point of the caudal needle seems to rest against bone it is well to withdraw it slightly. If blood is observed when the stilet of the caudal needle is removed, one may be quite sure that the plexus of veins which lines the bony canal has been punctured. Obviously intravenous injection results if the point of the needle lies in this plexus. A small hematoma may form in the caudal canal. It is said that the tip of the dural sac usually extends to the level of the second sacral foramen, and in a few instances I have obtained spinal fluid with the caudal needle at various levels, usually lower than the second sacral foramen and have produced spinal anasthesia. If spinal fluid appears, the needle should be withdrawn partially so that its point lies well below that of the dural sac, and a small amount, 5 to 10 c.c., of 1 per cent solution may be deposited in the bony canal. The principal part of the block should then be attempted by transsacral technique.

If no blood or spinal fluid appears when the stilet is withdrawn from the caudal needle, the syringe, not quite filled with procaine solution, is attached to the needle and gentle aspiration performed, first as the needle lies, and again after it has been given a half turn (180°). If no blood or spinal fluid appears on the first two aspirations, 0.5 c.c. of the solution is injected through the caudal needle and aspiration is repeated. If still no blood or spinal fluid appears, injection is continued very slowly so that the progress of the plunger through the length of the syringe is hardly perceptible. Twenty c.c. of solution is injected through the caudal needle, and this plus the 5 c.c. already injected through the 50 mm. needle brings the total thus far deposited in the canal to 25 c.c. During the while that the solution is being injected into the caudal canal through the caudal needle the tissue posterior to the sacrum is palpated. If solution is injected on the posterior surface of the sacrum there should be tumefaction or at least back pressure against the advancing piston.

When more than 25 c.c. is injected without a pause patients frequently complain of pain in the buttocks or popliteal spaces. When a complaint is made, the injection should be discontinued for a short period and then resumed slowly. Patients who give a history of sciatica are particularly susceptible to pain caused by pressure on the nerve roots. For these persons, slow injection throughout, interrupted by frequent pauses, is necessary.

In approximately 50 per cent of the patients, an area surrounding the anal orifice may be anesthetized completely by caudal injection alone, if 30 to 35 c.c. of solution of 1 per cent procaine has been injected and allowed to penetrate the nerve trunks for a period of thirty minutes. Frequently anesthesia may be incomplete, and it is necessary to inject the sacral foramina posteriorly. This is known as "transsacral block," and will now be described.

In order to find the lateral sacral foramina one must first palpate the posterior superior spine. In an obese subject the area immediately over this spine will be represented by a dimple; in a thin subject the bony protuberance can be easily felt; in the average subject it may be palpated by gentle pressure. In order to locate the bony point definitely, the fingers should be extended and held stiffly in that position and with a circular motion initiated from

the elbow, the area should be gently palpated, gradually, increasing the pressure of palpation. The first bony prominence encountered represents the posterior superior spine of the ilium. The point through which the needle entering the second sacral foramen should be inserted, is situated 1 cm. caudal and 1.5 cm. mesial to the posterior superior spine of the ilium. The landmarks for the first sacral foramen can be found 1 cm. cephalad and 1.5 cm. mesial to the spine. To find the point of entry of the needle reaching the third and fourth sacral foramina, the anesthetist should divide into three equal parts the distance between the landmarks for the needle entering the second sacral foramen and the point at which the caudal needle has already been inserted. The point of juncture between the upper and middle thirds is over the third sacral foramen, whereas the point of juncture of the middle and lower third is over the fourth sacral foramen.

Search for the third and fourth foramina is made by inserting a 50 mm. needle downward and inward until bone is encountered. The length of the shaft outside the skin is measured. The needle is partially withdrawn, its direction is changed slightly, and search is made for the opening. Finally, the sensation of the needle piercing a membrane will be experienced, and bone will not be encountered. The needle is inserted approximately 0.75 cm. deeper than that previously measured. The same procedure is followed for inserting a needle in the third foramen. For the second foramen, an 80 mm. needle is required. Search for the opening should be made with the angle between the needle in the hand, and the caudal needle already in place, approximating 90°. The needle for the first sacral foramen should be inserted at an even greater angle. Satisfactory anesthesia can usually be obtained by injecting on each side 10, 10, 3 and 2 c.c. of 1 per cent solution of procaine in the first, second, third and fourth foramina, respectively. Anesthesia develops within ten or fifteen minutes after injection and lasts for one or two hours.

During the past seven years there have been between 350 and 600 caudal transsacral blocks administered in this institu-

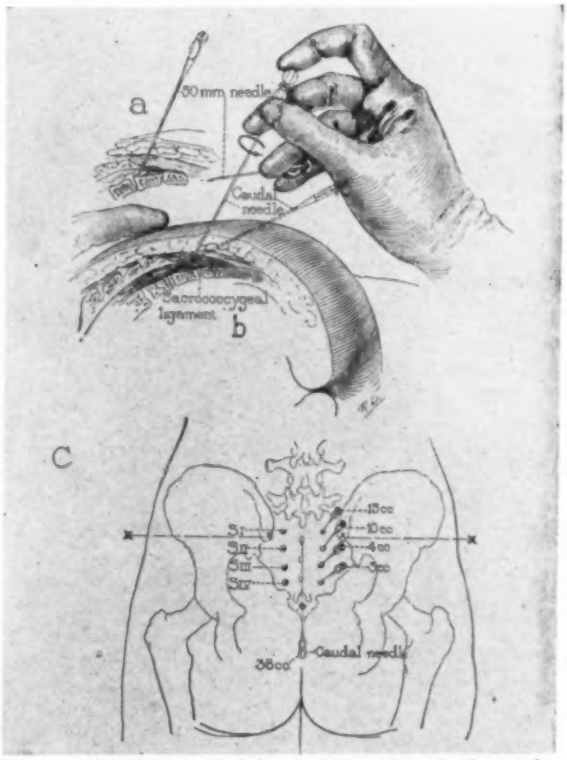


Fig. 2. *a*, A 50 mm. needle is inserted through a wheal over the sacrococcygeal membrane into the tip of the caudal canal and 5 c.c. of solution injected to make the insertion of the needle painless; *b*, the 50 mm. needle is withdrawn and the caudal needle inserted in its stead and advanced into the caudal canal, after being rotated so that the bevel rests on bone, and *c*, dorsal view of sacrum with caudal needle in position as well as those in SI, SII, SIII and SIV (the first, second, third and fourth sacral foramina). The maximal quantities that should be required for production of anestheisa in any case are indicated. (Tovell, R. M. in Curtis, Gynecology and Obstetrics. Vol. 3. Saunders, 1933.)

tion. They have been divided roughly into three main groups:

1. The urological service, 50 cystoscopies, 150 abdominal prostatectomies in which abdominal field block was employed, 47 transurethral resections;

2. Surgical service, 87 hemorrhoidectomies, 62 posterior resections, 94 fistulas and fissures, 17 Kraskes;

3. Gynecological service, 32 vaginal hysterectomies, 48 vaginal repairs, including perineorrhaphies, cystocele and rectocele, dilatation and curettage, 27 abdominal sections with abdominal field block, 10 cases in which there was partial or complete cardiac decompensation. These anesthetics were all administered by various members of the Department of Anesthesia.

Preliminary medication occupies a very important role in the success or failure of all local and regional forms of anesthesia.

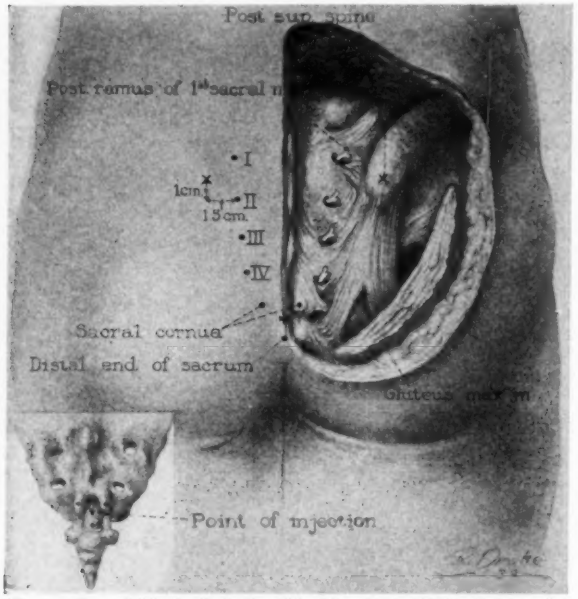


FIG. 3. Sacral block. Relationship of points of injection to the posterior superior spines, sacral cornua and distal end of the sacrum. The point of insertion of the caudal needle is the center of a triangle bounded by lines joining the sacral cornua and the distal end of the sacrum. (Tovell, R. M. in Curtis, Gynecology and Obstetrics, Vol. 3. Saunders Co., 1933.)

Its purpose is twofold, (1) to bring all patients as nearly possible free from fear and anxiety to surgery, and (2) to minimize against the convulsive symptoms in reaction caused by procaine or its derivates. The drugs most frequently used are in the order listed, barbituric acid derivates, opium derivates and scopolamine or hyoscine hydrobromide. The barbituric acid derivates divide clinically into two reactions, (1) sedative slow in action and long duration and (2) hypnotic rapid in action and short duration.[3] The opium derivates, of which morphine sulphate is the most common example, are all specific metabolic depressants (C. D. Leake) and are employed to allay pain. Scopolamine or hyoscine also lowers metabolism by reducing emotional excitement and produces amnesia which is most desirable. It also inhibits mucus secretion and in ordinary doses stimulates respiration.

With such potent weapons available patients who were considered poor subjects for this type of procedure may now be done with impunity. Our routine has been as follows: (1) Sodium amytal grs. 3 to 6 are given the night before at the hour of sleep. (2) In the morning one to one and a half hour before operation morphine sulphate gr. $\frac{1}{8}$ to $\frac{1}{4}$ depending upon age and weight, and scopolamine gr. $\frac{1}{200}$ to $\frac{1}{100}$, are administered. Thirty minutes before operation nembutal gr. 1.5 to 3, or seconal gr. 1.5 are given. In cases where the mentioned medication has not produced the proper amount of sedation as evidenced by emotional excitement, we resort to intravenous therapy, using a 10 per cent solution of pentothal sodium or evipal, either just before the block is to be performed or just prior to operation. The number of c.c. administered varies with the length of time desired to keep the patient quiet. We have used from 4 c.c. of pentothal to the full 10 c.c. or 1 gm. of the drug. While this much given intravenously may shorten the duration of the novocaine anesthesia, it does insure a quiet patient. We have also found intravenous pentothal a very desirable agent to complete a surgical procedure when the block begins to wear off before completion of the operation.

The agents employed during the first five years of this series of cases were 1 and 2 per cent novocain and pontocaine 0.1 per cent with 8 mm. adrenalin chloride 1–1000 in every 45 c.c. of agent employed. During the last year we have been using a solution containing 800 mgs. of novocain and 100 mgs. of pontocaine, with 8 to 10 mm. of adrenalin 1–1000 in 50 c.c. Since January 1, 1936, we have been using 800 mgs. of novocain, 100 mgs. of pontocaine, and cobefrin 1–2000 in the solution. While we have not had a sufficient number of cases to draw conclusions, isinteresting to note that there was less change in pulse rate and blood pressure with the cobefrin than when adrenalin or epinephrin were employed. In the majority of cases the amounts of fluid injected have been 25 to 40 c.c. of a 1 per cent solution in the caudal canal, and 8, 6 and 4 c.c. into the second, third and fourth sacral foramina, respectively, on each side.

Occasionally some unpleasant reactions occur in the course of injection or operation. The procaine reactions are of two

types, the first in which accidental injections of the solution into the blood stream occur, as mentioned in a previous paragraph, characterized by a fall in the blood pressure, slowing of the pulse rate, cyanosis, tremor and convulsions in which the patient may lose consciousness for a number of seconds, more or less, dependent upon the amount of agent injected. A milder attack occurs occasionally without intravenous injection and this may be observed by nausea and vomiting, clammy skin, slow pulse and faintness. The treatment for these unfortunate occurrences is first of all inhalations of oxygen and carbon dioxide or continuous oxygen while an intravenous of 10 per cent glucose 1000 to 1500 c.c. is being administered.[4] Waters has shown that in any circulatory collapse following subarachnoid block, better results are obtained if oxygen is employed immediately and continued during the administration of intravenous glucose before any cardiac stimulants such as adrenalin, caffeine, ephedrin, etc., are employed.

It can be seen from our results that this procedure is very valuable in the armmentarium of the anesthetists. It is regrettable that so many of our leading surgeons and anesthetists are satisfied with routine general anesthesia. While it is true that caudal transsacral block occasionally delays the operating room personnel as well as the surgeons and anesthetists, in selective cases time ought not to be a paramount factor. The procedure which is best suited for the patient is the one that should always be adopted. It has been our experience in this institution that the more selective the type of anesthesia for the individual case, the greater time saving for everyone concerned, as well as improved morbidity. We feel that in cases whereby this type of anesthesia is preferred, the operating room schedule can be so arranged that the block can be performed either before the operating room schedule has started, or while the surgeon is operating under some other type of regional anesthesia, such as subarachnoid block or epidural block after the technique of Dogliotti or Odom. It may be that the extradural technique described by Odom in this current issue may replace caudal transsacral block inasmuch as it definitely saves time and limits the number of needle punctures. While our experience with extradural block has been limited to approximately 200 cases it is interesting to note in comparison with caudal transsacral block for certain urological procedures, as transurethral resection, that we have had a certain amount of sphincter spasm while with caudal and transsacral anesthesia the relaxation is more complete. This sphincter spasm may possibly be attributed to anatomical abnormalities in which the novocaine does not reach all of the sensory nerves. The same might be said in regard to a limited number of partial failures when caudal alone is employed.

We have found this method of anesthesia exceedingly valuable on the urological, gynecological and proctological services, in old people who are essentially bad risks, patients suffering from acute and chronic hypertension and other vascular disturbances, and patients who refuse general anesthesia.

CONTRAINDICATIONS

The contraindications are relatively few, however one occasionally meets a patient who has had a very unpleasant experience with some other form of local or regional anesthesia, a patient's refusal, or an objective anatomical deformity.

CONCLUSIONS

1. Caudal transsacral block offers definite advantages in selective cases;
2. Routine anesthesia is inexcusable; and
3. All medical men specializing in this branch of medicine should be prepared to administer that type of anesthesia which is best suited to the patient, whether it be regional or general.

REFERENCES

1. Campbell, C. W. *Proc. Staff. Meet. of Mayo Clinic*, 12: 667–672 (Oct. 19) 1935.
2. Tovell, R. A. Anesthesia in Curtis, Gynecology and Obstetrics, vol. 3. Phila., W. B. Saunders Co., 1933.
3. Guedel, A. *Anesth. and Analg.*, 15: 159 (July-Aug.) 1936.
4. Seevers, H. M. and Waters, R. H. *J. A. M. A.*, 99: 961–968 (Sept. 17) 1932.

BRACHIAL PLEXUS BLOCK

EDWARD B. TUOHY, M.D.

Section on Anesthesia, The Mayo Clinic

ROCHESTER, MINNESOTA

THE success in blocking the brachial plexus depends largely on an accurate knowledge of the anatomic relationships in this region of the neck. Various methods of approach to the brachial plexus have been advocated, but it has been generally conceded that the supraclavicular approach of Kulenkampff and Persky[10] is the most useful and successful. The other methods which may be used are: (1) axillary (Hirschel[7]); (2) infraclavicular (Bazy and Blondin[1]); (3) paravertebral (Kappis[9]).

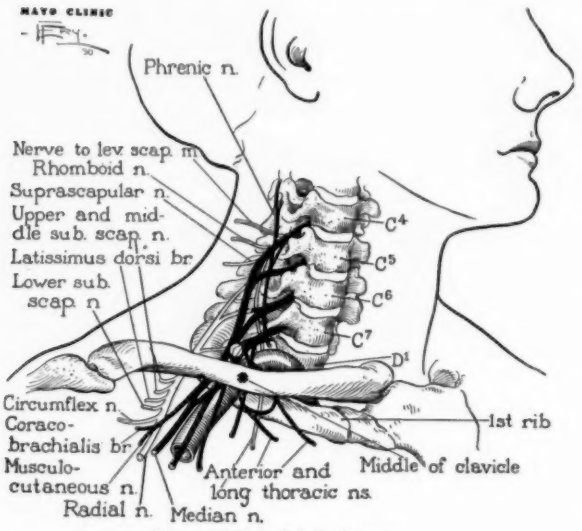


FIG. 1. Brachial plexus.

Essentially, the brachial plexus is composed of the anterior rami of the fifth, sixth, seventh and eighth cervical nerves, and the first and second thoracic nerves[3] (Fig. 1). The various nerves converge after leaving the intervertebral foramina and pass between the scalenus anticus and scalenus medius muscles, and lie close to the surface of the first rib. The various divisions then pass under the clavicle at its median point and enter the axilla. The supraclavicular branches supply the supraspinatus, infraspinatus, longus colli, levator scapula, rhomboidei major and minor, serratus magnus, and scaleni muscles, and the shoulder joint. The infraclavicular branches supply the teres major and minor, latissimus dorsi, and the greater and lesser pectoral muscles.

Of even greater technical importance than the anatomic formation and distribution of the plexus is the topographic relationship of the structures at the base of the neck. The main trunks of the plexus are bounded internally by the subclavian artery, externally by the clavicle, and below by the first rib. The subclavian artery lies alongside the plexus in the angle formed by the first rib and the clavicle, and is usually easily palpated with the finger since it is quite superficial. The middle point of the clavicle is found by measuring half of the distance between the acromioclavicular and sternoclavicular articulations. This point, as a rule, will correspond with a line projected from the external jugular vein toward the clavicle. At a point 1.5 cm. above the middle of the clavicle is the site at which the skin wheal is raised prior to blocking the brachial plexus.

INDICATIONS FOR BRACHIAL PLEXUS BLOCK

Livingston and Wertheim[13] advocated the use of this type of anesthesia in operations on severed nerves and tendons of the arm and hand, because it permits movements of individual groups of muscles. The method is obviously advantageous in cases in which anesthesia is desired in a limited region, and in cases in which it is desirable that there be a minimum of shock. Fractures and dislocations have been successfully treated by brachial block but in most cases general anesthesia in one form or another is preferred by the patients. Removal of foreign bodies deeply imbedded in the tissues of the arm and hand, and the plastic repair of Dupuytren's contractures are common examples of conditions which are well adapted to this type of anesthesia.

TECHNIQUE OF THE SUPRACLAVICULAR INJECTION

Most authors[4,5,6,8,11,14,15] agree that there are few disadvantages to this method of approach and that it is technically relatively easy to block the brachial plexus with this method (Fig. 2*a*). Labat[12] recom-

mended that the patient lie on his back with the head turned toward the side opposite the site of injection. The arm on the side on which the injection is to be made should be held close to the side of the body so as to depress the clavicle as much as possible. After the middle point of the clavicle has been ascertained, a wheal should be raised 1.5 cm. above it by injecting a 0.5 per cent solution of procaine hydrochloride. A 50 mm. needle of 20 or 21 gauge, unattached to a syringe, then should be gently introduced downward, backward, and inward (Fig. 2*b*). The patient should be instructed to tell the operator as soon as he feels any paresthesias in his arm and hand, because when these are elicited 20 c.c. of a 2 per cent solution of procaine hydrochloride with epinephrine 1:2600 should be injected without deflecting the point of the needle.*

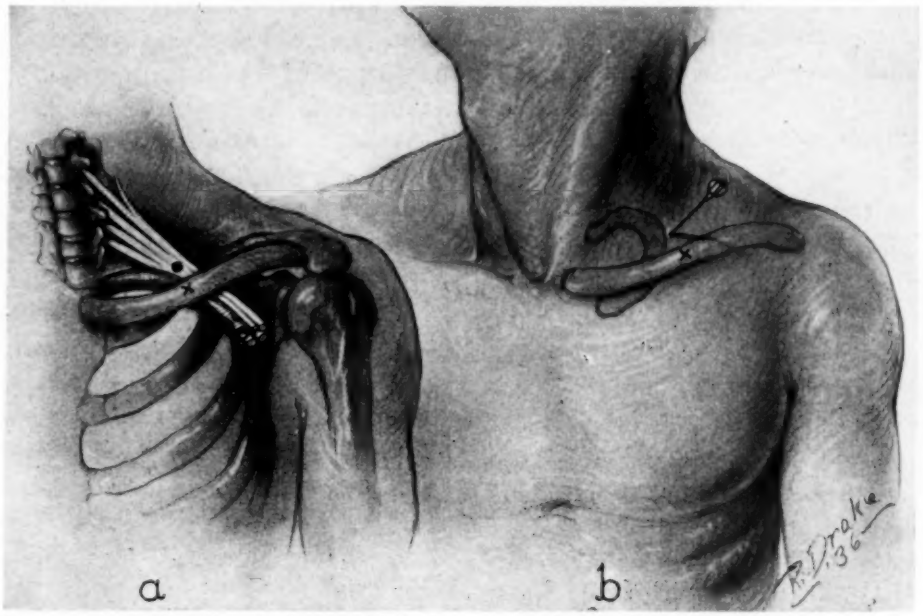


Fig. 2*a*. Relationship of the brachial plexus and the clavicle and subclavian artery: *X* marks the midpoint of clavicle and the dot and the site of injection; *b*, the relationship of the first rib to the site of injection.

If paresthesias are not obtained after the needle has been inserted 2.5 to 3 cm. it will ordinarily contact the upper surface of the first rib unless the general direction has been missed entirely. If the needle rests on the first rib and no paresthesias have been obtained, it is possible that it has passed between the branches of the brachial plexus without contacting them, and the needle should be withdrawn slightly changing the direction before reintroducing the needle. The usual error is that the needle has been placed too far laterally from the subclavian artery and clavicle in an effort to avoid the vessel. By compressing the subclavian artery with the index finger of the opposite hand and directing the needle closer to the clavicle, paresthesias will usually be obtained before contacting the rib again. In the absence of paresthesias, it is unwise to attempt multiple blind punctures in this region because of the danger of trauma to the blood vessels. Labat has suggested a technique that may be used when paresthesias cannot be obtained. This consists of injecting 10 c.c. of a 2 per cent solution of procaine hydrochloride beneath the fascia overlying the brachial plexus in the direction of the first rib, and supplementing this by injecting 5 c.c. of the same solution at the lateral margin of the first rib and 5 c.c. toward the transverse process of the sixth cervical vertebra. The supraclavicular region is then massaged gently for a few minutes in order to hasten diffusion.

When paresthesias have been produced, however, anesthesia of the arm and hand may be expected in fifteen to twenty minutes following the injection of 20 c.c. of 2 per cent solution of procaine hydrochloride. The duration of anesthesia is

* This solution is prepared by adding 5 c.c. of a 20 per cent solution of procaine hydrochloride to 45 c.c. of physiologic saline solution at a temperature of 35.7°C. One c.c. of a 1:2600 solution of epinephrine hydrochloride is added to the anesthetic solution.

usually one to two hours. In the event that only partial anesthesia of the hand, for example, is obtained, it is frequently possible to inject the solution into the nerve which supplies the unanesthetized region, near its termination or at the wrist. This is especially true for the median and ulnar nerves which are readily accessible at this point.

COMPLICATIONS

Perforation of any vessel will not cause much trouble provided that the needle used is not too large. If a hematoma forms it usually will reside subsequently without any residual effects. One must guard against the intravenous or arterial injection of procaine hydrochloride because this leads to possible convulsions if sufficient solution is introduced. If convulsive seizures occur they may be controlled by the intravenous administration of a barbiturate solution, such as pentobarbital sodium. The dosage depends on the severity of the convulsions and the age of the patient.

Perforation of the pleura may cause dyspnea and pain, but this difficulty is not encountered often if one is careful to inject the solution superficial to the first rib surface. Complete paralysis of an arm which lasted for five weeks has been reported by Boit,[2] while other authors have reported minor degrees of paresis of the arm with transient effects; these are all attributable to excessive trauma to the nerve trunks. Cases have been reported in which transient paresis of the phrenic nerve appeared fifteen minutes after injection of the solution and disappeared three or four hours later. Paresis of the sympathetic nerves in the neck and a contracted pupil may be observed occasionally.

CONTRAINDICATIONS

In cases in which there is evidence of disease of the nerve trunk, as in post-epidemic encephalitis and in other diseases in which there is involvement of the nerve trunks or infection in the supraclavicular region, it is not advisable to attempt to block the brachial plexus.

SUMMARY

The supraclavicular approach to the brachial plexus is probably the most useful and safest method of anesthetizing this area which has been suggested so far. It is especially well adapted for operations which are confined to the arm, forearm and hand, where it is desirable that the patient have control of motor function. The method is successful in 75 to 80 per cent of cases, provided there is close adherence to the proper technique. It should not be used in cases in which there is obvious disease of the brachial plexus or suppuration in the supraclavicular region.

The most serious complication which can result from this type of anesthesia is permanent injury to the brachial plexus; however, with careful technique trauma to these nerve trunks will be minimal.

REFERENCES

1. Bazy, L. and Blondin, S. L'anesthesie du plexus brachial. *Anestb. et Analg.*, 1: 190–198 (April) 1935.
2. Boit, Hans. Die Anästhesierung des Plexus brachialis nach Kulenkampff auf Grund von uber 200 Fällen. *Beitr. z. klin. Cbir.*, 93: 336–340, 1914.
3. Cunningham, D. J. Textbook of anatomy. New York, William Wood and Company, 1918, pp. 700–703.
4. Hanrahan, E. M., Jr. Brachial plexus block. *Virginia Med. Montb.*, 55: 305–306 (Aug.) 1928.
5. Harris, M. L. Local Anesthesia. Oxford Loose-Leaf Surgery. New York, Oxford University Press, vol. 3, pt. 1, 1918, pp. 122–126.
6. Hay, I. M. Brachial plexus anesthesia. *Jour. Florida Med. Assn.*, 15: 601–602 (June) 1929.
7. Hirschel, Georg. Die Anästhesierung des Plexus brachialis bei Operationen an der oberen Extremität. *München. med. Wchnschr.*, 2: 1555–1556 (July 18) 1911.
8. Hollingsworth, R. K. Regional anesthesia by nerve block method in reduction of fractures and dislocations. *Jour. Tennessee Med. Assn.*, 24: 294–299 (Aug.) 1931.
9. Kappis. Quoted by Labat. Regional Anesthesia. Its Technic and Clinical Application. Philadelphia, W. B. Saunders Company, 1928, p. 218.
10. Kulenkampff, D. and Persky, M. A. Brachial plexus anaesthesia: its indications, technique and dangers. *Ann. Surg.*, 87: 883–891 (June) 1928.
11. Labat, Gaston. Regional Anesthesia. Nelson's Loose-Leaf Living Surgery. New York, Thomas Nelson and Sons, vol. 1, 1927, pp. 551–553.
12. Labat, Gaston. Regional anesthesia. Its Technic and Clinical Application. Philadelphia, W. B. Saunders Company, 1928, pp. 215–238.
13. Livingston, E. M. and Wertheim, Hippolyte. Brachial plexus block; its clinical application. *J. A. M. A.*, 88: 1465–1468 (May 7) 1927.
14. Neil, W. F. and Crooks, Frederick. Supraclavicular anesthetization of the brachial plexus. *Brit. Med. Jour.*, 1: 388–389 (Feb. 22) 1913.
15. Rhone, T. B. Brachial plexus block anaesthesia. *Ann. Surg.*, 101: 1153–1170 (May) 1935.

EPIDURAL ANESTHESIA

CHARLES B. ODOM, M.D.

House Surgeon, Charity Hospital of Louisiana at New Orleans

NEW ORLEANS, LA.

THE surgeon of today realizes that no one anesthetic or method of anesthesia is applicable to every surgical case. He has found that each case must be approached as a distinct entity, and that the method of anesthesia requires as much meditation as the operative procedure to be used. At present every method of anesthesia has certain dangers associated with its use and these dangers are exaggerated in certain types of cases. It is true that some patients are poor operative risks no matter what type of anesthesia is used but this risk can often be lessened by the surgeon who is able to evaluate properly the particular type of anesthesia best adapted to the case. Every surgeon should acquaint himself with all the known types of anesthesia and become familiar with the advantages and disadvantages of each. With this in mind I wish to call to your attention a type of anesthesia which is relatively new in this country but which has been widely used in Europe and South America during the past four years with excellent results. The method is a form of block anesthesia which derives its name from the space into which the anesthetic solution is injected. As the epidural space extends the entire length of the spinal canal, it is possible through a single puncture to produce an analgesia sufficient to carry out any operative procedure below the chin without puncturing the dura and entering the subarachnoid space. For the past nine months I have been using this method and the results have been very gratifying. Particularly encouraging have been the results obtained with cases considered to be very poor risks for spinal or inhalation anesthesia.

Although this method of inducing anesthesia is relatively new, the idea of injecting anesthetic solution into the epidural space was first conceived by Corning in 1885, but he abandoned work along these lines to devote his time to the study and perfection of subarachnoid or spinal anesthesia. Six years later Cathelin blocked the last sacral and coccygeal nerves by injecting an anesthetic solution into the sacral canal through the sacral hiatus. In 1910 Lawen perfected this type of anesthesia which now is widely used in gynecology and obstetrics. Caudal or sacral anesthesia is an epidural type but its usefulness is limited to the perineum. Numerous attempts have been made to obtain abdominal anesthesia by injecting large quantities of anesthetic solution through the sacral hiatus with the patient in the Trendelenburg position. These results have been unsatisfactory and for practical purposes of little value.

The type of epidural anesthesia now in use was first conceived in 1920 by a young Spanish surgeon, Fidel Pagés. He found that the epidural space could be punctured in the lumbar and thoracic regions and thus anesthetize the abdomen and the chest. The career of this enterprising young man was unfortunately shortened by an untimely death from pneumonia. Not until ten years after Pagés' death is there any mention in the literature of epidural anesthesia, when, in 1931, Dogliotti reported before the Italian Surgical Congress the discovery of what he thought to be a new type of anesthesia. In comparing the reports of Pagés and Dogliotti one is struck by their marked similarity; however, Dogliotti does not mention Pagés, and I am sure he did not know of his work. At the American Congress of Anesthetists in 1932, Dogliotti reported his results with this method of anesthesia. The method

did not gain favor in this country; it is my opinion that at least one of the reasons was that Dogliotti described no definite means of localizing the epidural space.

Harger, of Chicago, in 1934 reported a series of 150 cases with very satisfactory results by the use of Dogliotti's method of lessened resistance. This method consists of engaging the spinal needle in the intraspinous ligament at the selected interspace and then removing the stylet. A 20 c.c. syringe is filled with anesthetic solution and then attached to the needle. As one hand slowly moves the spinal needle inward through the intraspinous ligament the other hand holds the syringe with the thumb on the piston exerting constant pressure. As long as the needle tip is in the ligament it is impossible to inject the solution because of the compactness of this structure. The moment the needle enters the epidural space this resistance is released and the plunger moves downward with ease. This method has its dangers because it is possible that the needle tip may be pushed just a little too far and puncture the dura, thus injecting the anesthetic solution into the subarachnoid space.

A definite method of localizing the epidural space was discovered in 1927 by Heldt and Maloney in experiments designed to show the cause of postlumbar puncture headaches. They reported the existence of a negative pressure in the epidural space, the cause of which has not as yet been explained satisfactorily. The most likely explanation is that when the back is bowed there is a stretching of the spinal canal which increases the space included within the potentially closed spinal canal and a vacuum results. This theory is supported by the fact that the greater the ability of the patient to arch his back the higher is the existing negative pressure. Although this negative pressure in the epidural space may be the cause of postlumbar puncture headaches it has proved of little value in their prevention, but Heldt and Maloney did not realize the usefulness of their discovery in anesthesia.

It remained for Gutierrez, of Buenos Aires, to recognize the value of a negative pressure in the epidural space. He devised a spinal needle with a concave top that would hold a drop of water. Upon puncturing the epidural space with this needle the water was immediately aspirated. This he designated "the sign of the drop" which is conclusive evidence that the tip of the needle is in the epidural space. Gutierrez has used this method of anesthesia in over 3000 cases and is very enthusiastic about its possibilities. I first saw epidural anesthesia given on Dr. Gutierrez's service at the Spanish Hospital in Buenos Aires and in my work have used his method with only a few variations.

In order to understand the effectiveness and safety of this new type of anesthesia it is essential to review the anatomy of the epidural space. The space extends the entire length of the spinal canal from the foramen magnum to the coccyx beginning above where the thick cranial dura splits at the foramen magnum into its two functionally different layers. The external layer lines the spinal canal as the periosteum and thick fibrous covering of the ligaments of the spine. In the region of the coccyx it becomes continuous with the periosteum of this bone. The anterior and posterior longitudinal ligaments are thick parts of this layer. The inner layer becomes the true spinal dura and covers the cord as a tubular sac. Between these two layers is a definite space, the epidural space, which contains semiliquid fat and venous plexus. The lower end of this space extends dorsalward to the sacral hiatus. This space is fairly large, and at the level of the second lumbar vertebra occupies approximately one-half the diameter of the spinal canal. The subarachnoid space is continuous above with the corresponding space of the brain. The epidural space, however, is found only in the vertebral column, its upper end being at the foramen magnum. This fact excludes the possibility of substances injected into this space getting to the medulla or the brain.

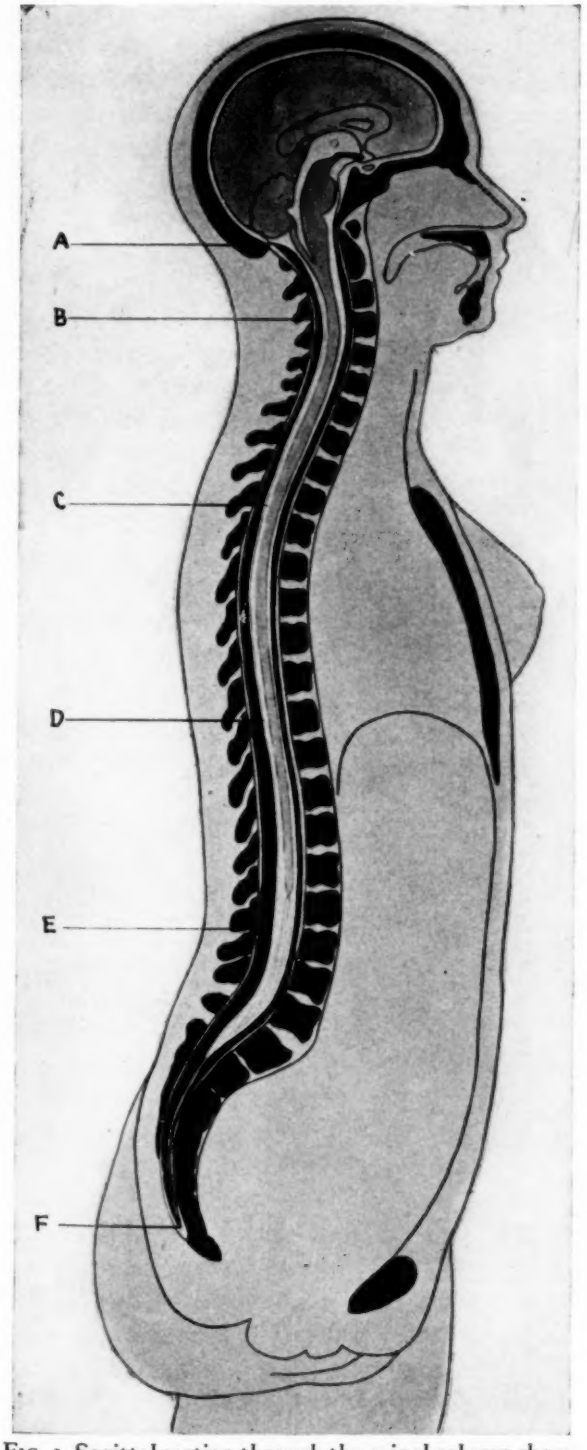


Fig. 1. Sagittal section through the spinal column showing location, size and limits of epidural space in dark black. *A*, upper limit at foramen magnum; *B*, outer wall of space formed by lining of spinal canal; *C*, subarachnoid space; *D*, spinal dura forming inner wall of epidural space; *E*, second lumbar interspace site of puncture, note relatively large size of epidural space at this level; *F*, sacral hiatus lower end of epidural space.

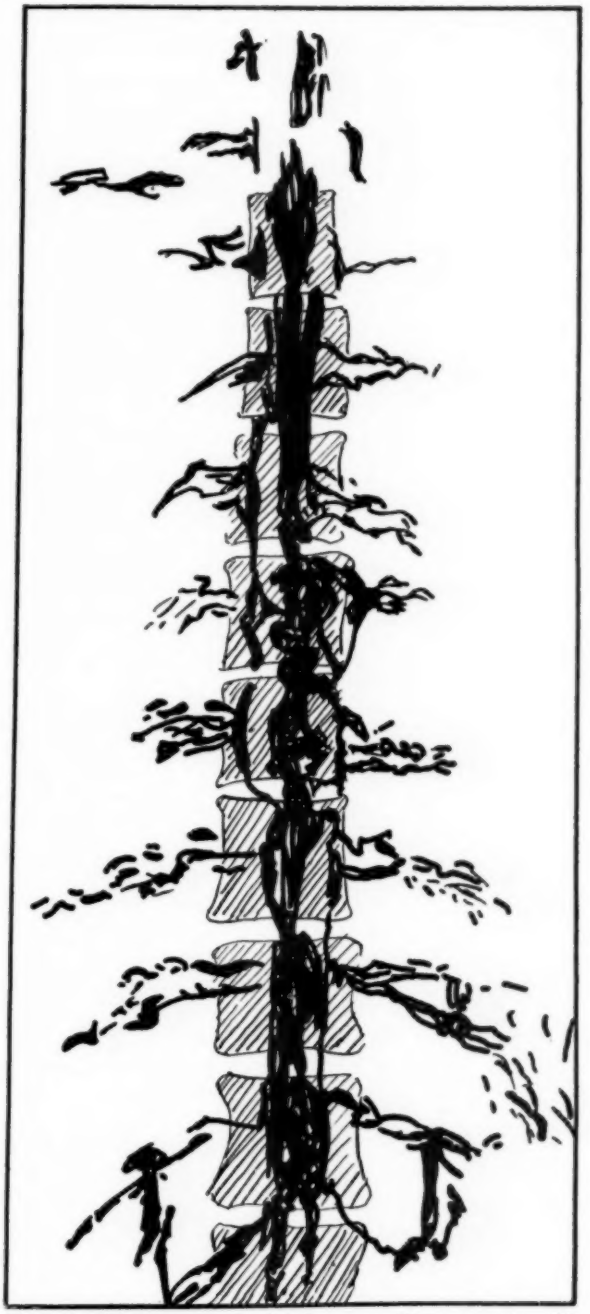


Fig. 2. Diagram of spinal column to illustrate the diffusion of anesthetic solution from epidural space. Note how the fluid leaves the epidural space at each intervertebral foramen along the perineural lymphatics. The resulting block is thus seen to be paravertebral. (This has been demonstrated by serial radiograms following lipiodol injections.)

The dura is continued as a covering of the nerves which emerge through it until just after the nerve leaves the intervertebral foramina. For this reason it is impossible for anesthetic solutions to block the spinal nerves within the epidural space. The injected solution infiltrates the semiliquid fat surrounding the dura and spreads both superiorly and inferiorly. At each intervertebral foramina some of the solution leaves the space along the perineural lymphatics surrounding the nerve trunks. It is in this manner that a massive nerve trunk block is accomplished which is comparable to a perfect paravertebral block.

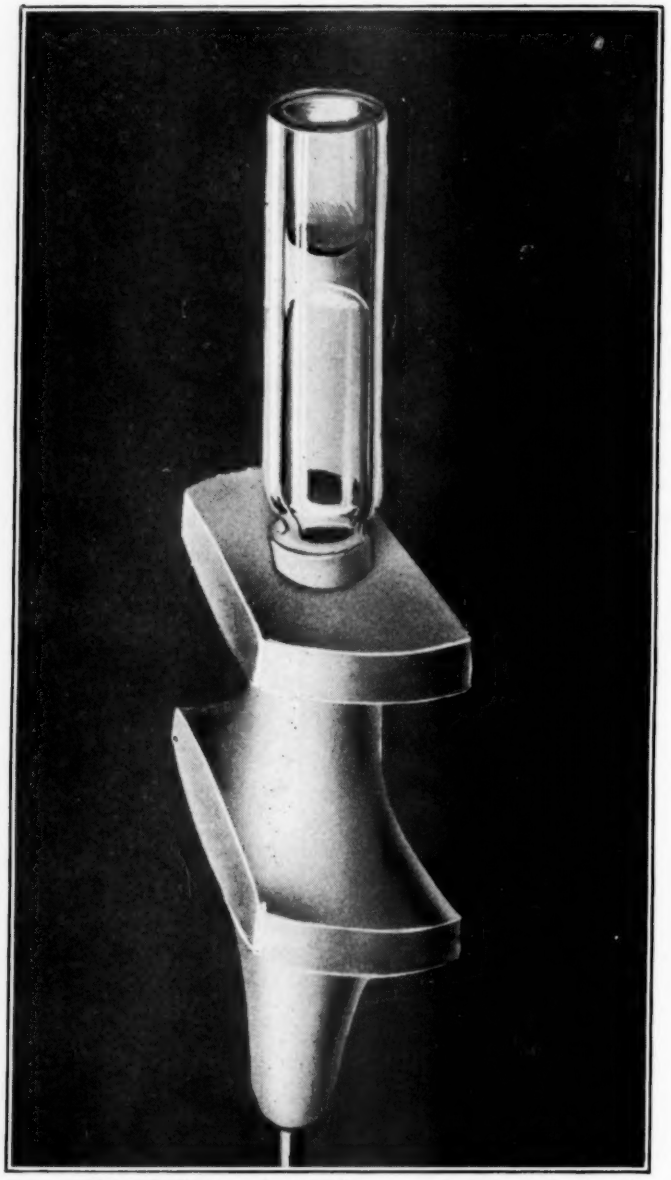


Fig. 3. Glass indicator devised by us to facilitate the localization of the epidural space through the negative pressure method; the lumen of the indicator is filled with water.

Thus we see that the anesthesia is entirely of the nerve roots outside the spinal canal and there is no contact whatsoever between the anesthetic solution and the central nervous system.

The path followed by solutions injected into the epidural space was first definitely proved by Forestier who injected solutions, such as lipiodol, and then took serial

radiograms of the spinal column. The opaque substance was seen to infiltrate the epidural space and then pass from the spinal canal through the intervertebral foramina until at the end of several hours the entire amount of lipiodol was outside the vertebral column.

ARMAMENTARIUM

The necessary materials are very simple and present in every hospital.

1. A 2 c.c. hypodermic syringe and needle for producing a skin anesthesia at puncture site;
2. A 20 gauge short bevel spinal needle;
3. A 20 c.c. syringe for injecting the solution;
4. A large medicine glass;
5. The anesthetic solution of choice;
6. A small glass indicator.

This indicator has proved of great value in localizing the epidural space. In my first cases of this type of anesthesia I found it difficult to keep a drop of solution in the top of the spinal needle which I used. Following the suggestion of Dr. Graffagnino I cut a small glass adapter, (Luer connecting tip #420ST) commonly used to connect a rubber infusion hose to an infusion needle, in half and connected it to the spinal needle after it had been engaged in the intraspinous ligament. The ground glass tip of the adapter made the connection air-tight. The lumen of the adapter was then filled with sterile solution. This small glass cylinder with the enclosed fluid made a very delicate indicator. The smaller the bore of the cylinder the more delicate it becomes. This indicator is very easily sterilized and is far less cumbersome to use than the spinal manometers or U tubes used in some of the European clinics. Depending upon the height of the negative pressure in the epidural space the fluctuations of the fluid in the indicator may vary from a slight vibration to complete aspiration. Likewise a positive pressure will be registered and the fluid forced outward should a vein be punctured or the tip of the needle be accidently pushed into the subarachnoid space. For those who find the movement of a clear solution hard to follow it is possible to fill the indicator with a colored solution such as methylene blue.

TYPE AND AMOUNT OF ANESTHETIC SOLUTION

It is possible to use any type of anesthetic solution in epidural anesthesia that has been safely used in local anesthesia. The two important factors which one must always bear in mind are as follows:

1. The anesthetic solution must be of sufficient concentration to penetrate through the thick neural sheaths which exist in the paravertebral region; for this reason the solutions used must be of slightly higher concentration than that used in local anesthesia.

2. A sufficient quantity of the solution must be injected to insure contact with and blockage of all the sensory nerves supplying the operative field. In my first series of cases I attempted to use solutions of 1 per cent and 1.5 per cent novocaine and found that this concentration was not high enough. My results did not become uniform until I began using a 2 per cent solution of novocaine which was prepared from crystals just before injecting. I added 10 mm. of adrenalin in order to slacken the rate of absorption of the novocaine by causing a vasoconstriction of the vessels in the region injected and thus lessen the toxicity of the novocaine as well as prolong the length of the anesthesia. I saw several cases in this series with minor reactions such as pallor of the face, tachycardia and complaints of dizziness, which were attributed to the adrenalin and ceased following its discontinuance. At the present time I add adrenalin in only the very poor risk cases and then use only 5 or 6 minims. The solution is prepared in a large medicine glass from sterile novocaine crystals using normal saline as a solvent. I usually prepare 50 c.c. of the solution and vary the amounts injected in the following manner:

35 c.c. for inguinal hernioplasties, appendectomies and lower limb operations;

45 c.c. for gynecological surgery;
50 c.c. for upper abdominal procedures such as cholecystectomy and gastric surgery.

Shortly after completing my first series of cases I began searching for an anesthetic solution which would give prolonged anesthesia without the addition of adrenalin. I found the solution desired when I combined pontocaine with novocaine. This combination has proved extremely satisfactory and will give an anesthesia lasting from one and a half to two hours. As far as I have been able to determine this is the first time this combination has been used in epidural anesthesia. The solution is made up just before injecting by dissolving 500 mg. of novocaine and 100 mg. of pontocaine crystals in 50 c.c. of normal saline. The novocaine and pontocaine crystals are now available in 500 mg. and 100 mg. ampoules respectively. The resulting 50 c.c. solution has a concentration of 1 per cent novocaine and ⅕ per cent pontocaine.

One of the objections which has been raised to this type of anesthesia is that the dosage of novocaine used is too high. The amount of novocaine crystals in 50 c.c. of a 2 per cent solution is 1 gram, which is the maximum dosage used. It must be remembered that this type of anesthesia is in no way comparable to spinal and the dosage used is more nearly comparable to local anesthesia. In local anesthesia this dosage of 1 gram is often exceeded. Braun states that 2 grams of novocaine is the maximum amount that should ever be employed; therefore half that amount would certainly seem to be within safe bounds. Larger dosages than 1 gram with no ill effects have been reported by Dogliotti and Caporale. Peham and Americh in their high sacral anesthesia use 1.5 grams of novocaine with no evidence of overdosage.

TECHNIQUE

The position in which the patient is placed is extremely important in this type of anesthesia. This is readily apparent to those who are experienced with spinal anesthesia. The patient may be either seated on the operating table or may lie on one side, depending upon the position preferred by the operator. I prefer to have my patient lying down and use the sitting position only in cases in which it is difficult to arch the back. The side on which the incision is to be made is always placed down to take advantage of the gravitation of more of the anesthetic solution to that side. The body is brought to the edge of the operating table with the back slightly bowed. The shoulders and hips should be in a vertical line, for tilting of either results in the "corkscrew spine" and makes puncture difficult. The lower back is then cleansed with an antiseptic solution. The second lumbar interspace is located by palpation and marked with the thumbnail. At this site in the midline using the 2 c.c. hypodermic syringe an intracutaneous injection of a small quantity of novocaine solution is performed. Through this wheal the 20 gauge spinal needle is then introduced until its tip is well engaged in the interspinous ligament. The stylet is withdrawn and the small glass indicator is connected to the spinal needle and filled with solution. An assistant then arches the back of the patient by bringing the chin down onto the chest and flexing the thighs and the legs. This causes a stretching of the spinal canal and increases the negative pressure in the epidural space. The back should not be arched before everything is in readiness for the puncture as an inflow of blood into the peridural venous plexus might dilate the veins and compensate in part for the increased negative pressure and at the same time increase the likelihood of venous puncture.

With the back arched the spinal needle is slowly pushed through the interspinous ligament. At the point where the needle punctures the yellow ligament a snap is felt and the point of the needle enters the epidural space. At this same instant the fluid in the indicator will be sucked into the needle because of the negative pressure in the epidural space. This is conclusive evidence that the tip of the needle is in the

epidural space and the anesthetic solution can be injected with ease and safety. The 20 c.c. syringe is then connected to the

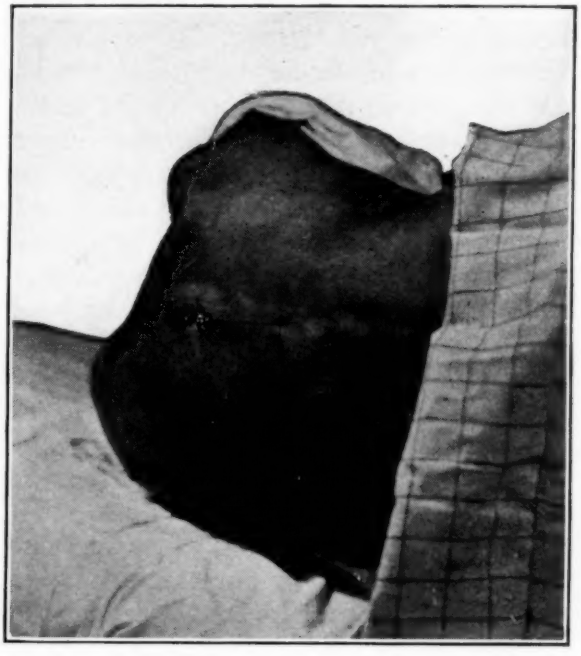


Fig. 4. The patient is shown in correct position with the back arched and spinal needle in the epidural space at the level of the second lumbar interspace.

needle and 10 c.c. of the anesthetic solution is slowly injected. The fluid flows in freely with as little resistance as in intravenous injections. A period of five minutes is then allowed to elapse. This precaution should always be followed by those individuals not experienced in giving this type of anesthesia as it completely obviates the possibility of an accident from subdural injection of the solution. At the end of this period the sensibility of the lower extremities is tested and if the patient has no anesthesia and can move his legs one may be certain that the needle is not in the subarachnoid space and can proceed to inject the remainder of the solution. If the 10 c.c. of solution has been accidently given into the subarachnoid space an ordinary spinal anesthesia will result. The solution should be injected slowly, a short time being allowed to elapse between each 20 c.c. to allow for diffusion of the solution.

Following the injection of the solution the patient lies flat upon the table. If the operation to be performed is in the pelvis or lower extremities the patient is placed in Fowler's position to facilitate gravitation of the solution downward and block-

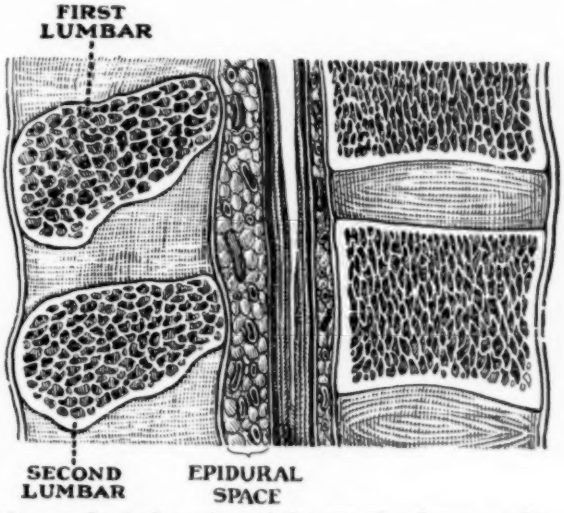


Fig. 5. Sagital section of the spinal column at the level used for puncture of epidural space. Note the size of the epidural space, subarachnoid space, and spinal cord.

age of the sacrococcygeal nerves. A slight degree Fowler's position is also indicated in inguinal hernias and appendectomies to prevent the upward diffusion of the anesthetic. On the other hand a slight Trendelenburg position should be used when anesthesia of the upper abdomen and chest is desired. In kidney operations the patient should lie for fifteen minutes on the side on which the operation is to be performed so that the greater amount of solution gravitates to that side.

Pagés and Dogliotti in some of their work attempted to obtain a "segmental anesthesia" by injecting the solution in the region of the nerves supplying the segment of the body in which the operation was to be performed. Thus they varied their site of puncture, at times tapping the space in the lumbar region, dorsal or cervical regions. This is technically more difficult than the method we now use and one is more likely to get incomplete anesthesia. I routinely use the second or third interspace in the midline as this is the most desirable site for puncture for the following reasons:

1. At this level the epidural space is larger; therefore it is easier to tap and

there is very little danger of puncturing the dura.

2. The spinal processes come off in a horizontal plane in the lumbar region and with the back arched there is a definite widening of the interspace and a puncture can be made easily and painlessly. In the dorsal spine the processes come off in a more vertical plane, making puncture difficult.

3. From this level it has been found by observation that anesthesia of any desired level can be obtained by taking advantage of gravity.

4. Puncture is made in the midline because there is less danger of injuring the endorrhachial veins which are lateral.

MANAGEMENT OF THE PATIENT

The results of this anesthesia as in any other type of nerve block depends a great deal upon the proper management of the patient. He should be told in advance of the type of anesthesia that is to be used, its advantages, and the sensations he will be likely to experience. Thus the patient's frame of mind is important; he should go to the operating room with thorough confidence in his surgeon and in the anesthetic to be used. A neurotic patient or one who is particularly desirous of being asleep during the operation should not be given this or any other nerve block anesthesia unless it is absolutely necessary. One-half hour before the operation the patient should be given morphine ¼ gr. and sodium luminal, 2 gr. These drugs will tend to allay fear and apprehension. In cesarean sections no preoperative medication is used.

During the operation an assistant or anesthetist properly trained in the psychological management of patients should always be at the head of the table. Such an assistant will take a great burden from the surgeon's shoulders as well as make the patient comfortable and unapprehensive. Often this assistant will succeed in absorbing the patient's attention to such an extent that he will not know the operation is in progress. The surgeon and his assistant should be careful of what is said as the patient is easily excited and will remember everything that occurs.

Reaction to Anesthetic Solution. If the correct technique is used the patient experiences no discomfort whatsoever while the solution is being injected. In a few cases, probably due to an idiosyncrasy of the patient, there might be such symptoms as pallor and sweats which are purely nervous phenomena as they have been found to occur following simple puncture of the skin. Nausea occasionally occurs and is undoubtedly due in most cases to a slight sensitivity of the patient to novocaine. This is always transitory and soon disappears. Immediately after the injection in most cases there is a slight increase in the pulse and respiratory rates. The tachycardia is exaggerated when adrenalin has been added to the anesthetic solution.

Blood pressure changes are relatively slight in this type of anesthesia and therefore one of its advantages. In those cases where the anesthesia is limited to the abdomen there is little or no fall in blood pressure. When the block includes the chest and neck the fall in pressure is gradual and at the end of twenty minutes usually varies from 20 to 30 mm. systolic and 10 to 20 mm. diastolic. In a few cases the fall was slightly greater but never enough to cause the patient discomfort or worry about his well being.

During the period of waiting for the onset of anesthesia the patient should be kept whenever possible in a room entirely separate from the operating room.

Within ten minutes after the injection a band of anesthesia appears in the lower abdomen which corresponds to the area supplied by the nerves nearest the sight of injection. This band slowly widens until it has spread up into the chest and down into the legs. The usual height to which the block extends is just below the clavicles. However, in a number of cases the anesthesia spreads up to the chin, and yet these patients are perfectly comfortable. The explanation of this is apparent when one reviews the neurological findings. Usu-

ally within fifteen minutes complete surgical anesthesia is obtained. In some cases it is necessary to wait as long as twenty-five or thirty minutes. The anesthesia lasts one and one-half to two hours, not including the period of onset. It disappears gradually from the periphery and last from the central zone of anesthesia.

A point which I cannot stress too strongly is that the surgeon should wait fifteen or twenty minutes before beginning the operation. It must be remembered that the anesthetic solution must diffuse around the nerve trunks and then penetrate their thick sheaths before anesthesia is complete. Too early a start before anesthesia is complete may cause the patient to be apprehensive throughout the operation.

NEUROLOGICAL FINDINGS

In this type of anesthesia the sensory nerves are completely blocked but the motor nerves are very little, if at all, affected. For this reason the intercostal and the phrenic nerves are not blocked even when the anesthesia has spread as high as the chin. Likewise not a single case under my observation lost the ability to move his legs. This selectivity of the sensory nerves cannot be explained upon an anatomical basis as the anterior and posterior nerve roots are joined within the dura and this block is carried out extradurally. The most likely explanation is that the anesthetic solution has a selective action on the sensory fibers and respects the motor fibers. Even though the motor roots are not blocked the abdominal muscles are completely relaxed. The relaxation is comparable to the type obtained with spinal anesthesia. This is due to the fact that the nerve reflex has been interrupted at one point of its sensory pathway. Another point as important to the surgeon as relaxation is that all visceral sensibility is lost, thus facilitating abdominal exploration. The patient experiences no discomfort when traction is used on the gall bladder or stomach. This is due to a blockage of the rami communicantes.

From the central zone of anesthesia the sensation of pain is the first to disappear. Temperature sensibility is next lost and

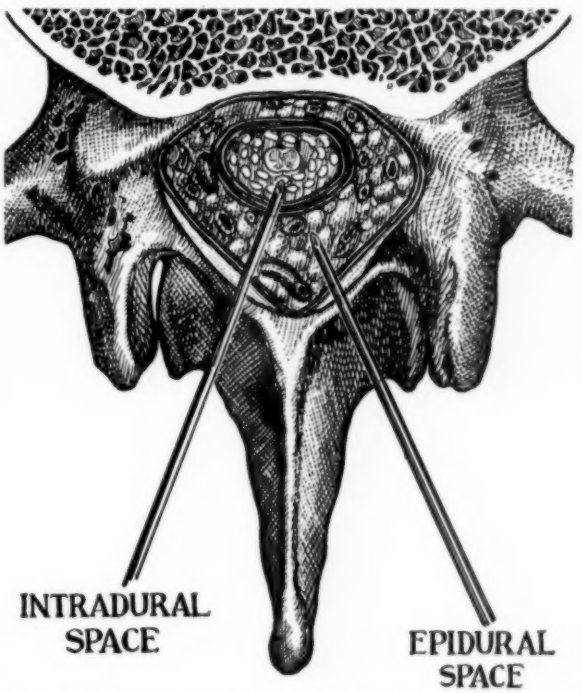


Fig. 6. Transverse section of the spinal canal at the level of the second lumbar vertebra. Note the size of the epidural space which makes it relatively easy and safe to tap. The needles demonstrate the difference in position of needle tip for spinal and epidural injections.

last to be blocked is the tactile sense. In some cases the sensation of touch is not lost completely and as a result the patient is aware of the operation but experiences no pain. The cutaneous and deep reflexes of the abdomen are completely absent. The knee jerk also is lost. The achilles reflex, however, is always present, which proves the contention that the reflex arc is always broken in the sensory pathway.

ACCIDENTS

In this type of anesthesia there are two possible types of accident: first, that in which the anesthetic solution may be injected into the subarachnoid space rather than the epidural space, resulting in an overdosage of spinal anesthetic; and second, hypersensitivity of the patient to the anesthetic solution. This second possibility at present cannot be avoided, but it is hoped that at some time in the near future

an anesthetic drug of very low toxicity will be discovered which will obviate this danger. The first mentioned cause of accidents should never occur, and I believe will not occur if the operator is always careful of his technique. With the negative pressure method the epidural space can be definitely and safely localized. The five minute period following injection of the first 10 c.c. should always be reserved by those not familiar with the method as an interval of waiting. This serves as an additional safeguard against subarachnoid injection. A last precaution to which resort can be made when in doubt as to the position of the needle is repeated attempts at aspiration while injecting the solution.

There was one case in this series in which I think at least part of the 50 c.c. of 2 per cent novocaine was injected intradurally. It was my tenth case and up to that time I had not taken the precaution of waiting after injecting the first 10 c.c. The case was that of a very emaciated negro male, fifty-three years of age, who had a ruptured appendix with localized peritonitis, and who had been vomiting for several days. Seven minutes after injection of the anesthetic solution the patient's respiration ceased. He was given artificial respiration and after fifteen minutes began to show signs of recovery. During this interval his pulse remained good although there had been a marked drop in the blood pressure. Within thirty minutes the patient had completely recovered. He was returned to the ward and treated conservatively using Ochsner's technique. He was discharged from the hospital in two weeks in good condition.

The wide variety of operative procedures possible under this type of anesthesia is evidenced by the following series of the past nine months:

Appendectomies	32
Cholecystectomies	11
Cholecystostomies	2
Cholecystoduodenostomies	2
Hernioplasties.	
Incarcerated inguinal	10
Inguinal	7
Bilateral inguinal	3
Umbilical	4
Epigastric	1
Femoral	4
Ventral	6
Gastrostomies	6
Gastroenterostomies	4
Subtotal gastrectomies	4
Enteroentrostomies	3
Ileostomies	2
Fistulectomies	2
Hemorrhoidectomies	4
Mastectomies	2
Rib resections	3
Resection of rectum	1
Reduction of fractures of lower extremities	4
Splenectomies	1
Excision of pilonidal sinus	2
Prostatectomies	2
Suprapubic cystostomies	3
Total cystectomy	1
Hysterectomies.	
Supravaginal	21
Vaginal	2
Perineorrhaphies	12
Conization of cervix	9
Dilatation and curettage of uterus	12
Laparotomies.	
Exploratory laparotomies	6
Volvulus of sigmoid	3
Traumatic abdomen with rupture of bowel	1
Pistol shot wounds of abdomen	3
Stab wounds of abdomen	2
Drainage of acute hemorrhagic pancreatitis	1
Intestinal obstructions	5
Ruptured peptic ulcers	8
Ruptured ectopic pregnancies	5
Presacral sympathectomy	1
Myomectomy of uterus	1
Uterine suspensions	8
Salpingo-oophorectomies	8
Cesarean sections	14
Obstetrical deliveries, normal and abnormal	37
Total	285

This series though not adequate on which to base any definite conclusions will give an idea of the possibilities of the wide application of this type of anesthesia. The most important point which this series proved was that epidural anesthesia can be used with safety in a group of cases which are extremely poor risks for other types of anesthesia. It was possible to carry out necessary operative procedures in a number of aged individuals with arteriosclerotic heart disease and hypertension. Cesarean sections were performed on 2 women with advanced pulmonary tuberculosis, 2 with advanced myocardial disease and one with diabetes mellitus. Both mothers and babies did extremely well.

Another group in which epidural anesthesia is indicated are those cases which are already in shock and therefore should be spared as much additional shock from the anesthetic as possible. Included in this group are ruptured peptic ulcers, ruptured ectopic pregnacies, and gun shot wounds of the abdomen.

In order to give an idea of the usefulness and safety of this type of anesthesia a few briefly summarized cases are presented.

Case I. Mrs. J. G., aged forty-four years, weight 359 pounds, mild hypertension, with diagnosis of umbilical hernia, multiple uterine fibroids, chronic appendicitis, chronic cholecystitis and cholelithiasis, was on the operating table for two hours. A supravaginal hysterectomy, bilateral salpingo-oophrectomy, appendectomy and hernioplasty were performed. The patient made an uneventful recovery, and left the hospital at the end of two weeks in good condition.

Case II. Mrs. W. H., aged sixty-three years, hypertensive heart disease with chronic nephritis and a surgical diagnosis of intestinal obstruction of forty-eight hours' duration. At laparotomy a volvulus of the sigmoid was reduced and a sigmoidopexy performed. The patient recovered.

Case III. Mrs. R. S., aged sixty-eight years, marked progressive distention of the abdomen with severe abdominal pain; blood pressure 250/160. A laparotomy was performed and two large malignant papillary cystadenomas of both ovaries were removed. The tumors weighed twenty pounds. Following operation the patient had complete relief from pain although not cured of her condition.

Case IV. Mr. J. S., aged sixty-two years, chronic nephritis with mild hypertension and a surgical diagnosis of chronic calloused ulcer of pylorus with obstruction. A posterior gastroenterostomy was successfully performed.

Case V. Mrs. J. G., aged thirty-nine years, weight 315 pounds; surgical diagnosis of umbilical hernia and adenoma of right breast. A hernioplasty and resection of the right breast were performed. The patient had an uneventful recovery.

Case VI. Mrs. D. D., aged thirty-eight years; surgical diagnosis of pistol shot wounds of the abdomen with perforation of the ileum, duodenum and left kidney. A portion of the ileum was resected, perforations of the duodenum were repaired and a left nephrectomy were performed. The patient recovered.

Cases VII, VIII and IX. Mr. W. T., aged sixty-seven years, Mr. L. J., aged seventy-two years, and Mr. J. B., aged seventy-five years. All had strangulated inguinal hernias which required resection of the gangrenous loop of ileum. All went through the operation with no ill effects and had uneventful recoveries.

Case X. Mrs. F. H., aged forty-eight years, myocardial disease with hypertension, marked obesity; surgical diagnosis of intestinal obstruction of four days' duration due to constriction around the pedicle of a large ovarian cyst, and a ventral hernia. The obstruction was reduced by removal of the ovarian cyst and the ventral hernia was repaired. The patient had a smooth convalescence.

Thirty per cent of the cases in this series were emergency procedures and patients of this type are usually much poorer operative risks than are elective cases. In spite of the large number of these poor risks there was only one death in which there was a possibility that the anesthetic was responsible. The case was that of an eighty-two year old female with a strangulated ventral hernia of seven days' duration. She was in very poor condition when placed on the operating table but it was felt that the only chance the patient had was through operative intervention. Twenty minutes after the anesthetic had been administered the patient expired. Cardiac stimulants and artificial respiration were used to no avail. Gutierrez in his series of 3000 cases reports 2 fatalities. Both were in people over sixty years of age, one with mitral stenosis and the other with a marked cardiac arrhythmia.

FAILURES

The vast majority of cases in which epidural injection fails to give complete surgical anesthesia are due to faulty technique. A secondary cause might be attributed to anatomical abnormalities of the spinal canal which prevents proper diffusion of the anesthetic solution. The use of too dilute an anesthetic solution or an insufficient quantity to block all the nerves

supplying the operative field are also causes of a resulting incomplete anesthesia.

I am convinced that faulty technique plays the major role because I have been able to reduce my number of incomplete anesthesias from 9 per cent in the first 100 cases to 5 per cent in the last 100 cases. Included in these failures are all cases in which a supplementary anesthesia, ether, ethylene or evipal, had to be used.

COMPARISON WITH OTHER TYPES OF ANESTHESIA

When epidural anesthesia is compared with other types its advantages are readily seen. It has all the advantages of spinal anesthesia without many of its undesirable features. There is no danger of injuring the cord as the dura is not punctured; bulbar accidents cannot occur because the anesthetic solution cannot reach the medulla; spinal anesthesia affects the central nervous system whereas epidural anesthesia blocks only the nerve roots; since the dura is not pierced there is no danger of meningitis or encephalitis; blood pressure changes are less marked than in spinal; a longer anesthesia can be obtained with epidural than with spinal; patients are more comfortable and vomit less often.

When compared with general anesthesia it is found that epidural anesthesia is less toxic and it is possible to use this type of block in cases with pulmonary and cardiac complications in which general anesthesia is definitely contraindicated. A well trained, skilled anesthestist is always necessary to give a good general anesthetic whereas epidural anesthesia can be given by the surgeon.

Patients in which epidural anesthesia is used are far more comfortable postoperatively than after any other anesthesia. There is no nausea or vomiting. Headaches and neck pains which one encounters so often in spinal anesthesia do not occur. Another postoperative finding of no little importance is the fact that following epidural anesthesia the patients are able to void voluntarily and very infrequently does one have to be catheterized.

SUMMARY

Although I do not feel that epidural anesthesia is the ideal type, I believe it has numerous advantages particularly in those cases usually considered to be poor operative risks. From this series no definite conclusions can be drawn, but it is certain that epidural anesthesia has not received the attention in this country which it deserves. It should be made part of the armamentarium of every anesthestist and general surgeon.

Although there are dangers in its administration, care coupled with the negative pressure technique all but obviates them.

The fact that one must wait fifteen to twenty minutes after injection for the anesthesia to become effective makes it probable that epidural anesthesia will not be widely used in busy hospital services. However, the advantages of epidural anesthesia more than compensate for this period of waiting.

REFERENCES

Caporale, L. Peridural segmentary anesthesia in renal surgery. *Jour. Urol.*, 35: 403–408, 1936.

Corning, J. L. Spinal anesthesia and local medication of the cord. *New York Med. Jour.*, 42: 483–485, 1885.

Dogliotti, A. M. Segmental peridural spinal anesthesia. *Am. Jour. Surg.*, 20: 107–118, 1933.

Gutierrez, Alberto. Anesthesia metamerica peridural. *Rev. de Cir. de Buenos Aires*, 11: 665–685, 1932.

Gutierrez, Alberto and Rubido, M. L. Resultados obtenidos con la anesthesia peridural. *Rev. de cir. de Buenos Aires*, 12: 90–101, 1933.

Harger, John. Peridural anesthesia in abdominal surgery. *Illinois Med. Jour.*, 65: 317–319, 1934.

Heldt, T. J. and Moloney, J. C.: Negative pressure in epidural space. *Am. Jour. Med. Sc.*, 175: 371–376, 1928.

Heldt, T. J. Lumbar puncture headache. *Med. Jour. and Rec.*, 129: 136–139, 1929.

Hess, Elmer. Epidural anesthesia in urology. *Jour. Urol.*, 31: 621–628, 1934.

Odom, C. B. A review of Pagés epidural anesthesia with a report of 100 cases. *New Orleans Med. and Surg. Jour.*, 88: 618–627, 1936.

Pagés, Fidel. Metameric anesthesia. *Rev. san. mil. Lima*, 11: 351–365, 385–396.

Peham, H. and Amreich, J. Operative Gynecology, vol. 1, 1934, pp. 36–68.

Ruiz, Vincente. La anesthesia peridural de Pagés en ginecologia. *Rev. méd. latino-am.*, 20: 233, 1935.

Soresi, A. L. Preliminary report on epidural anesthesia. *Med. Jour. and Rec.*, 135: 165–166, 1932.

INTRAVENOUS ANESTHESIA

JOHN S. LUNDY, M.D.

Section on Anesthesia, The Mayo Clinic

ROCHESTER, MINNESOTA

IN a recent article Magill, celebrated anesthetist of London, made the statement that "the barbiturates are the only agents which can be regarded as of practical value for intravenous use at the present time."[28] The intravenous method of administering an anesthetic agent has a very strong appeal to the experienced anesthetist, especially if he has had considerable experience in the administration of drugs, and especially in the intravenous administration of anesthetics. When skillfully used, the method has advantages which make it the method of choice in many instances.

The progressive development of the intravenous method has been no more rapid than has the introduction of better and better drugs for this purpose. Chloral hydrate was used intravenously as an anesthetic in 1872 by Ore,[31] of Lyons, France. This is the first record of general anesthesia produced by the intravenous injection of an anesthetic drug. Hedonal was first produced by Dreser, of Munich, in 1899. Hedonal was used intravenously as a general anesthetic by Krawkow, of Petrograd, in doing experimental work between 1905 and 1908, and in 1908 he introduced hedonal-chloroform narcosis.[20] Ether and chloroform were used by Burkhardt. He first used chloroform in 1909 but soon discontinued that and began the use of a 5 per cent solution of ether in physiologic saline solution and reported very satisfactory results. The use of paraldehyde was reported in 1913 by Noel and Souttar,[30] who used 5 to 15 c.c. of paraldehyde mixed with an equal quantity of ether, dissolved in 150 c.c. of 1 per cent solution of sodium chloride. Graef[13] in 1913 reported 151 cases in which ether anesthesia was induced intravenously and 359 cases in which anesthesia was induced with a 1.5 per cent solution of trichlorisopropyl alcohol (isopral) and maintained with a 5 per cent solution of ether in normal physiologic saline solution. Both drugs were administered intravenously. Magnesium sulphate was used by Peck and Meltzer[32] in 1916, and they described 3 cases in which the drug had been used intravenously to produce anesthesia. Marin,[29] of Mexico City, in 1929, reported the use of 96 per cent ethyl alcohol in a 25 per cent solution of dextrose intravenously as an anesthetic. In 1929 Constantin reported two successful administrations of ethyl alcohol intravenously[8] and 40 cases[9] in 1930. Somnifene, a mixture of diethyl barbituric acid and allylisopropyl barbituric acid, was used intravenously by Fredet and Perlis[12] for general surgical anesthesia in 1924. Cleisz[7] reported on the successful administration of somnifene in obstetric cases the same year. The use of ipral was reported in 1925 by Jackson and Lurie.[15] In 1927 Bumm[5] described general surgical anesthesia produced by the intravenous injection of pernocton. Bosse[4] and others reported several hundred cases in which it was used successfully. Petit and Perlis[33] reported the intravenous administration of allonal to dogs in 1926 and Keller,[18] in 1927, reported 70 cases in which allonal was administered intravenously to produce anesthesia. Kirschner,[19] in 1929, reported the intravenous use of a 3 per cent solution of avertin in 150 cases.

In 1929, Zerfas and others[39] reported on the induction of anesthesia in man by the intravenous injection of sodium amytal. In 1929, I[21] reported 273 intravenous administrations of the drug for surgical anesthesia, with untoward results confined largely to the postoperative period. Sodium

amytal is now used for the control of various conditions and especially as an antispasmodic but it is not recommended for surgical anesthesia. Sodium embutal (pentobarbital sodium, nembutal) I found to be better than sodium amytal for surgical anesthesia and in 1930 I[22] reported on 52 cases in which it was administered intravenously. Although its action is shorter than that of sodium amytal, its effect is still too prolonged to warrant its continuous use as a surgical anesthetic. Evipal soluble, introduced in 1932 by Weese and Scharpff,[38] was by far the best agent for intravenous anesthesia that had yet been introduced, and since that time a voluminous literature has been developed. In 1934 I used clinically pentothal sodium (thionembutal) and reported on it later in some detail.[23–27] In 1935 Döring,[10] of Berlin, reported 600 cases in which general anesthesia had been induced since 1933 by intravenously administering eunarcon (the sodium salt of isopropyl-B-bromallyl-N-methyl barbituric acid). In 1936 Thalheimer[36] reported the use of 1-methyl-5, 5-allyl-isopropyl-barbituric acid (narconumal) in 500 cases with fair results.

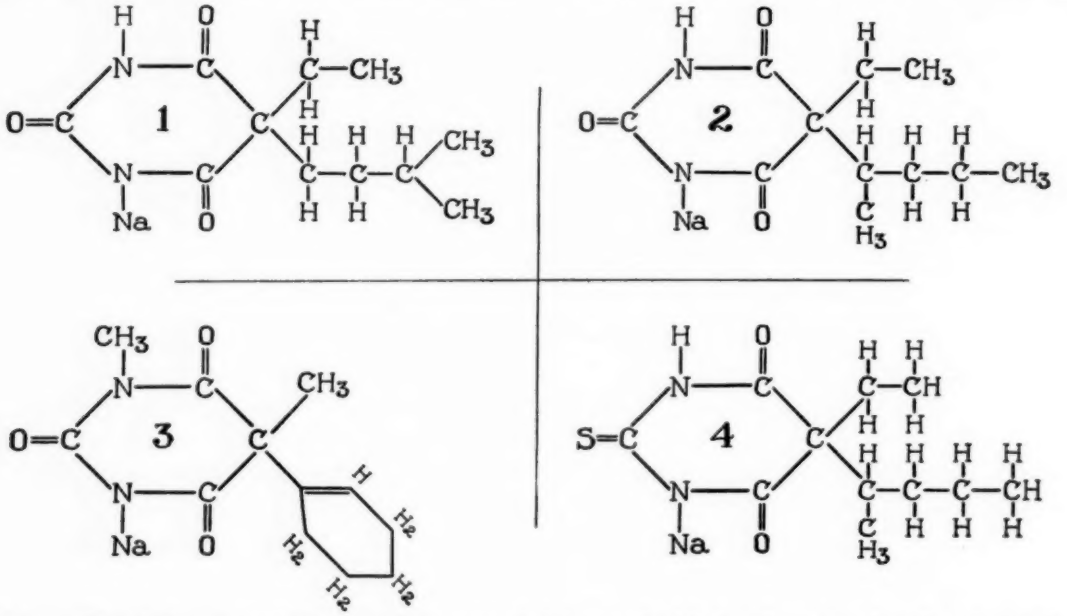


Fig. 1. Chemical structures of (1) sodium amytal, (2) pentobarbital sodium (nembutal), (3) evipal soluble, and (4) pentothal sodium. Sodium amytal and pentobarbital sodium are similar in chemical structure and they have a similar effect. Evipal soluble and pentothal sodium, although differing somewhat in chemical structure, have a similar effect. The one difference between the latter two and the first two substances is the utilization of bonds on the urea side of the barbituric acid nucleus as well as on the malonic acid side for substituent radicals in the formulas for evipal soluble and pentothal sodium, while in the formulas for sodium amytal and pentobarbital sodium the bonds on the malonic acid side only have been utilized. (Hutton and Tovell. *Surg., Gynec. and Obst.*, accepted for publication.)

Each time a known anesthetic agent was introduced it seemed that the best one possibly had been discovered; however, most of these agents have been discarded later because of untoward results in the hands of experienced anesthetists. However, evipal soluble and pentothal sodium are so definitely superior to the drugs previously used that intravenous anesthesia has been definitely established on a basis that seems firm enough so that I look for a rather continued use of the method.[16,34,35] I have previously commented on the use of these two drugs and the literature is abundantly supplied with articles on evipal soluble. Therefore, it seems to me that my remarks should be confined largely to the less known agent, pentothal sodium, although the results obtained with the two agents are similar.

Pentothal sodium is definitely more potent than is evipal soluble and for that reason is more satisfactory when one must anesthetize a resistant individual. With both agents induction of anesthesia is quick, maintenance of anesthesia appears to be similar, and recovery is rapid.

Barbiturates which are injected intravenously may be divided into three classes according to the different effects that they produce, that is, a prolonged, sustained, or transient effect. Sodium amytal produces a prolonged effect, pentobarbital sodium (nembutal) produces a sustained effect, and pentothal sodium and evipal soluble produce a transient effect (Fig. 1).

ADMINISTRATION

It is important to stress the fact that the original technique that was advised in the use of evipal soluble was to inject a quantity of solution sufficient to produce anesthesia, then to inject a similar amount because it was assumed that the patient could safely tolerate at one time twice the amount of the drug necessary to produce anesthesia, and finally to withdraw the needle. It is only because of the inherent virtue of the drug itself that it was able to survive this abuse. It seemed to me, because of the evanescent effect of the anesthetic, that it would be well to administer the drug intermittently. This technique is the one I have used and I think it is preferable.

In the early use of these drugs they were administered in solutions of 10 per cent concentration. Occasionally, the patient complained of soreness at the site of injection, especially if some of the drug had been injected extravenously. There occasionally was clotting of blood in the needle, but recently I have been using pentothal sodium in 5 per cent concentration and have avoided these conditions, in all except one case where a vein was used on the back of the hand. Microscopically, the erythrocytes are apparently unharmed after blood has remained in a syringe for

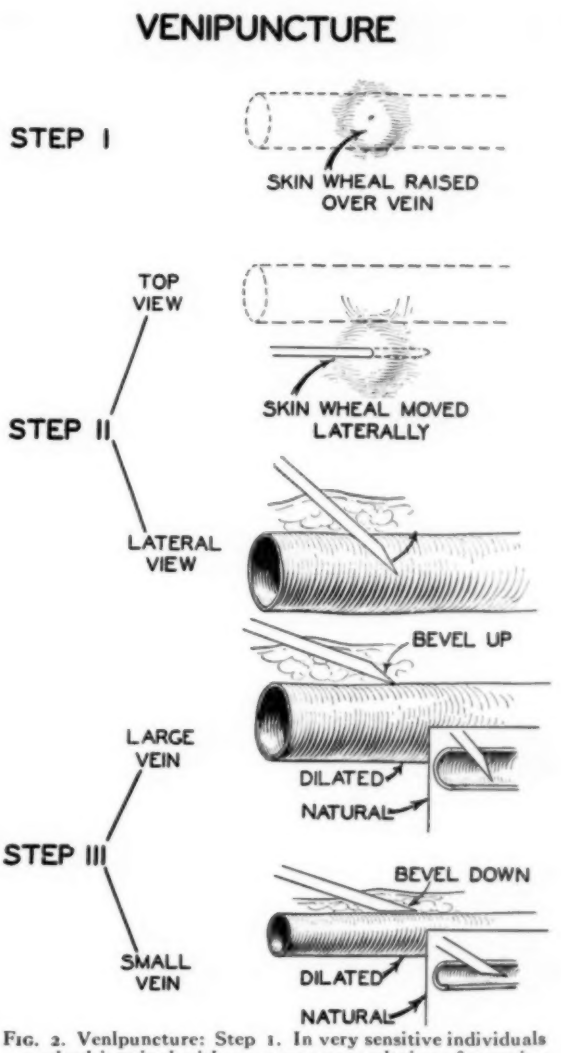


Fig. 2. Venlpuncture: Step 1. In very sensitive individuals a wheal is raised with a 0.5 per cent solution of procaine in the skin overlying the vein. For the majority of adults this step is unnecessary. Step 2. The next procedure is to thrust the needle through the skin, not attempting to enter the vein with the one motion, but rather to move the skin which overlies the vein laterally. Then move the skin back so that the needle lies against the side of the vein. Step 3. Move the skin into position so that the needle overlies the vein. With the constrictor in place the vein is dilated. If the vein is large the point of the needle lies entirely within the lumen even when the vein is not dilated. On the other hand, when the vein is very small, the point of the needle will not lie free in the lumen of the vein when the vein is not dilated, unless the bevel of the needle is held as shown.

It is important to use mild negative pressure in the syringe as soon as the point of the needle has been thrust into the skin. Also a counter-pull must be used on the vein with the hand that does not hold the syringe. By a right-handed person, the syringe is held by the right hand and the needle inserted through the skin. The right fingers grasp the plunger and the tip of the right thumb is placed against the edge of the barrel in order to produce the negative pressure. The fingers of the left hand are pressed against the skin overlying the vein at a point far enough from the spot where the needle enters the skin so that the left hand in no way interferes with bringing the needle and syringe flush with the patient's skin. Unless this counter-pull with the left hand is employed, venipuncture may become very difficult, especially in veins around the wrist and in the hand, because they are movable and must be fixed if they are to be easily entered by the needle. This counter-pull must be exactly opposite to the direction of the insertion of the needle.

a period of hours with either a 5 or 10 per cent solution of pentothal sodium.

The skin is surgically prepared and venipuncture is carried out at a place which permits the anesthetist to be away from the operative field and in a position to observe the patient's respiration. In every method of anesthesia, there is a part of the technique which may be difficult in certain cases. Obviously, with intravenous anesthesia venipuncture is essential and in those cases in which patients have veins that are not suitable, the method may be contraindicated. Because of the difficulty that might be encountered in inserting the needle into the vein, the technique of venipuncture must be mastered by the anesthetist in order to reduce the number of times that he otherwise would be unable to use the method. The technique of venipuncture applies not only to intravenous anesthesia but also to intravenous medication and blood transfusion (Fig. 2).

A dorsal metacarpal vein in the back of the hand is often convenient to use although venipuncture may be easier at the elbow, using the median basilic vein or the median cephalic vein. When a vein at the elbow is to be used, an arm board may be used with a strip of adhesive tape over the patient's wrist and around the board to keep the patient from bending his arm. Various types of drapes may be used. Towels are usually employed, although a thick drape with a perforation about 2 inches in diameter is useful. Occasionally, it may be desirable to use a vein in the ankle. In such instances, the one injecting the solution must be kept informed by the individual sustaining the patient's jaw if respiration becomes too greatly depressed at any time. The anesthetist, when administering an intravenous anesthetic in a vein of the ankle, has difficulty in watching the motion of the cotton butterfly overlying the patient's nostrils as the patient's head is out of sight, when a mirror is not available. The anesthetist may snap his fingers once to let the attendant at the head of the table know that he wants to be sure the patient is breathing properly. The attendant then holds a hand above the drapes and bends a finger to simulate the motion of the cotton both as to rate and degree. When a vein in the ankle is being used, it is important to know whether or not varicose veins are present. If they are, care must be exercised to massage the vein frequently from the ankle toward the knee to speed the passage of the drug into the general circulation; otherwise, an overdose may be suddenly administered.

When surgical anesthesia is produced, respiration is considerably depressed, and

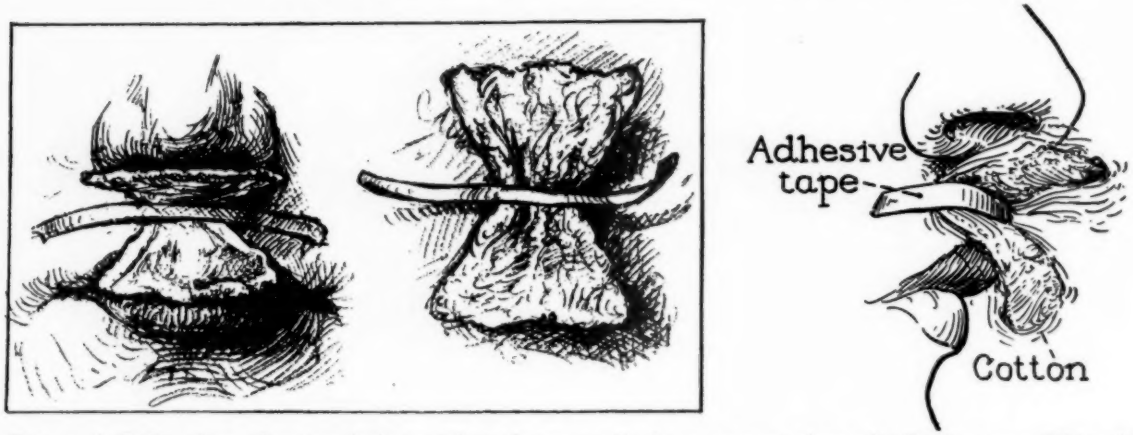


FIG. 3. A fluffy piece of cotton is fastened to the upper lip by a narrow piece of adhesive tape. This will indicate, by its motion, that the air passage is patent and is functioning. Patency of the airway must be maintained by sustaining the lower jaw. The barbiturate should be injected intravenously slowly enough so that the motion of the cotton does not stop. This is more easily accomplished if a respiratory stimulant is administered with the barbiturate. (Lundy. *Engineering Chem. Jour.*, 28: 1031–1034 [Sept.] 1936.)

in an attempt to minimize this depression various respiratory stimulants have been incorporated in small amounts in the anesthetic solution in 1395 of the cases included in Table 1. One of the stimulants is coramine which is a 25 per cent solution of pyridine betacarbonic acid diethylamide. One cubic centimeter of coramine, containing 250 mg. of pyridine betacarbonic acid diethylamide, is added to each gram of pentothal sodium. A respiratory stimulant is used particularly in those cases in which preliminary medication has been administered. Preliminary medication usually consists of the administration of 1.5 grain (0.097 gm.) of pentobarbital sodium (nembutal) by mouth and the administration of $\frac{1}{6}$ grain (0.01 gm.) of morphine sulphate and $\frac{1}{150}$ grain (0.0004 gm.) of atropine hypodermically one hour before operation. In order to know that the airway is free I have fashioned a piece of cotton as illustrated in Figure 3. The absence of motion of the cotton indicates that respiration has been depressed to an undesirable degree or that the airway is not free. I attempt to administer the anesthetic slowly enough so that the motion of the cotton is not stopped. I feel that when this is accomplished carefully the use of the drug in properly selected cases is relatively safe.

Table 1
INTRAVENOUS ANESTHESIA WITH PENTOTHAL SODIUM*
(June 18, 1934 to November 1, 1936)

	1936	1935	1934
Operations on brain, spinal cord and peripheral nerves	149	76	3
Operations on eye	68	52	20
Operations on head and neck (other than the above)	271	276	9
Dental extractions	23	32	2
Transurethral and cystoscopic operations and manipulations	644	458	25
Orthopedic operations	107	44	1
Operations on thorax, thoracic wall, breast and axilla	247	158	1
Digestive system operations	12	9	0
Operations on the large bowel	85	40	7
Intra-abdominal operations	6	8	0
Operations on abdominal wall and for hernia	42	23	
Gynecologic operations	469	147	4
Operations on anus	57	10	1
Total	2207	1333	73

* Distribution of cases in which pentothal sodium was used either to induce anesthesia or maintain it, according to the type of operation that was done.

When the anesthetist has no assistant available to sustain the patient's jaw, various devices have been suggested to permit intermittent administration of the drug and yet leave the anesthetist's hands relatively free most of the time for duties other than the actual injection.[14,17] I have not found such devices necessary as I prefer to have experienced individuals in charge of the syringe as well as to sustain the jaw. My method of preparing the solution is first to aspirate the respiratory stimulant into a 20 c.c. syringe, then to aspirate about 10 c.c. of sterile distilled water into the syringe, and to discharge this mixture into the ampoule containing 1 gm. of pentothal sodium. In a few moments the drug is dissolved and this mixture is then aspirated into the syringe, following which an additional amount of sterile distilled water, sufficient to bring the contents of the syringe to 19.5 c.c., is aspirated, using a long, large bore needle to facilitate reaching to the bottom of the large ampoules. The large needle is then replaced with a 20 gauge, short bevel, $1\frac{1}{2}$ inch needle. This small needle is capped with the empty sterile ampoule which contained the respiratory stimulant, in order to protect the needle when it is carried from place to place before the injection is made and also to indicate the kind of respiratory stimulant in the solution so that it is easily recognized by whoever administers the drug. I prefer to use a glass syringe with an eccentric tip. The golden color of the solution, which is easily seen, is attributable to the sulphur in the pentothal sodium (Fig. 1) and it is an aid in recognizing the content of the syringe. There is also a definite and characteristic odor to the solution. Occasionally, a patient will mention an unusual taste in

his mouth during the first part of the induction period.

Because of the short period of induction of anesthesia with pentothal sodium, injection of the drug is not begun until just before the incision is to be made. It is desirable to have the bladder and rectum empty and it is important that the stomach is empty. If any stomach contents are regurgitated into the throat, laryngeal

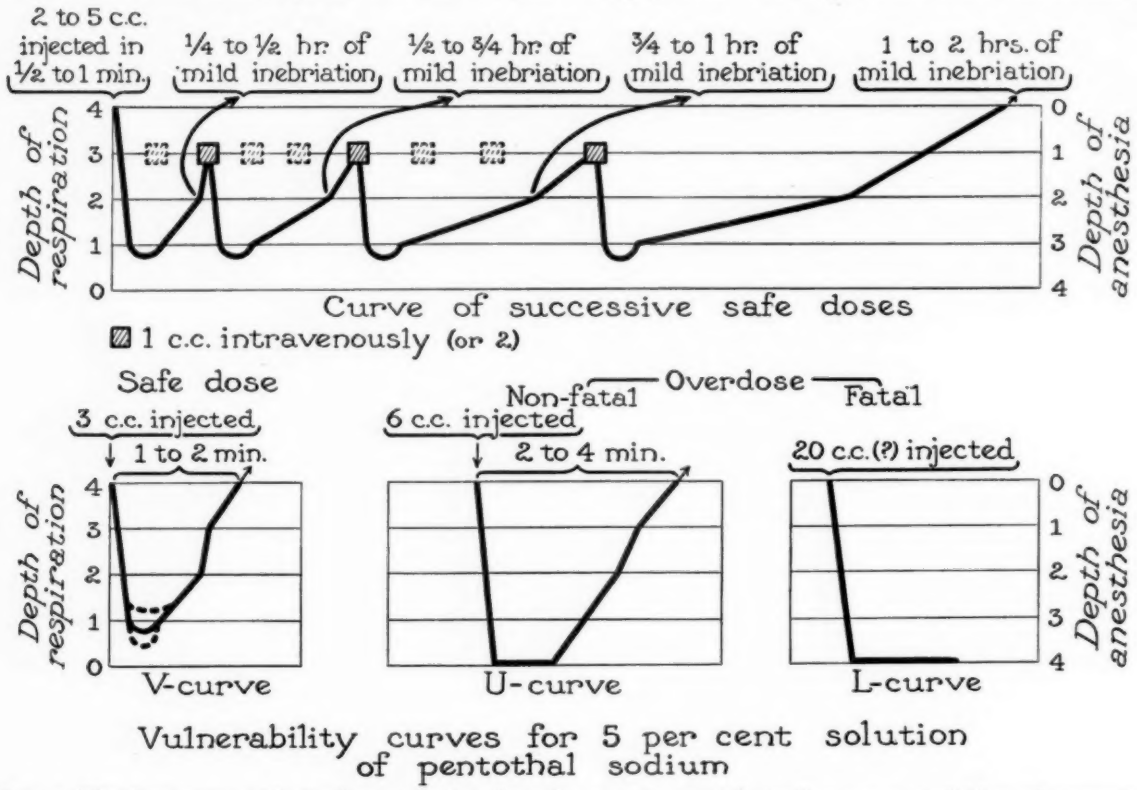

2 to 5 c.c. injected in ½ to 1 min.
¼ to ½ hr. of mild inebriation
½ to ¾ hr. of mild inebriation
¾ to 1 hr. of mild inebriation
1 to 2 hrs. of mild inebriation
Depth of respiration
Depth of anesthesia
Curve of successive safe doses
1 c.c. intravenously (or 2)
Safe dose
Non-fatal
Overdose
Fatal
3 c.c. injected
1 to 2 min.
6 c.c. injected
2 to 4 min.
20 c.c.(?) injected
V-curve
U-curve
L-curve
Vulnerability curves for 5 per cent solution of pentothal sodium

Fig. 4. The intravenous dose of pentothal sodium for a man, aged forty-five years, weighing 160 pounds (72.6 kg.); height 6 feet (182.9 cm.); preliminary medication consisted of ⅙ grain (0.01 gm.) of morphine and 1/150 grain (0.0004 gm.) of atropine by hypodermic injection and 1.5 grain (0.097 gm.) of pentobarbital sodium orally.

Effect produced by the administration of pentothal sodium by different techniques. To avoid the necessity of drawing two curves in each diagram it is assumed that anesthesia deepens as respiration becomes more shallow and that this relationship between the two is exact. The relationship may not be exact but for diagrammatic purposes the assumption will serve. The top diagram gives the effect on depth of respiration and of anesthesia produced by repeated safe doses. After the first dose, respiration becomes more shallow and anesthesia deeper for a time; then, as the patient begins to recover, respiration deepens and anesthesia lightens until the patient reaches a stage of inebriation which will last for a fourth to half hour. If the operation has been completed in the relatively short period of anesthesia conferred by the first dose, no more of the drug need be administered and after the stage of inebriation has passed, recovery is complete. However, if a longer period of anesthesia is required to permit the operation to proceed, a second dose is administered and so on, with the effects on respiration, anesthesia and duration of inebriation that are represented in the curve. When similar successive safe doses are administered, the last one often has a longer effect than the previous ones. The dosage varies with individuals according to their resistance to the drug. One may require 2 c.c. of solution for each 1 c.c. as indicated in the top curve, at least for the first two or three injections.

The diagrams marked V-curve, U-curve, and L-curve show the relative effect of the safe dose and of the overdose. The V-curve illustrates the safe dose for the short operation, for example, manipulation of a stiff wrist joint. The U-curve illustrates the nonfatal result of a moderate overdose; respiration is practically completely depressed for a short time and the recovery is prompt if no more of the drug is injected. It shows that the period of anesthesia is longer than it is when a small dose is injected and this period of anesthesia is coincidental with respiratory depression. The overdose, that is, one large enough to be fatal, is illustrated in the L-curve and needs no further explanation. Certain modifications of this technique might be carried out and the L-curve could be broken down into two U-curves the second of which might possibly illustrate a fatal result, based on the results obtained in the top curve or if complicated by any respiratory obstruction.

spasm may develop, and if it does, difficulty will arise in ventilating the patient. Although it is easily possible to shorten the period of induction to ten seconds, it is safer in most cases to take at least thirty seconds to induce anesthesia. Within that period of time the anesthetist will have discovered the probable tolerance or resistance of the patient to the drug. From 2 to 5 c.c. of a 5 per cent solution of pentothal sodium is usually sufficient for induction of anesthesia (Fig. 4). Occasionally, as much as 0.5 gm. is required. I usually precede the injection by aspirating 0.5 c.c. of blood into the syringe to test the sufficiency of the venipuncture. I then inject 1 c.c. of solution to prove that the vein has been properly entered and to see that an extravenous injection will not occur. Occasionally, this small dose has been almost enough to produce mild surgical anesthesia in an aged, infirm, small person. After a period of a half minute or a little less elapses following the injection of 1 c.c. of solution, I feel that I have some information concerning the probable effect of small quantities of the drug on the patient. The patient is asked to count as soon as one has finished the injection of the first dose of 2 or 3 c.c. Most patients count at least to ten. If there is no apparent effect at the count of fifteen, 1 c.c. of solution is injected and if the effect is still mild, another cubic centimeter is injected on the count of twenty, and so on, injecting another cubic centimeter on the count of twenty-five and perhaps another on the count of thirty. When counting ceases and the patient is well asleep, the surgeon should test the skin with a sharp instrument before the actual incision is made. If the patient responds to the stimulation of the incision by moving or phonating, one or two additional cubic centimeters of the solution of pentothal sodium should be injected. Once anesthesia has become established and the incision has been made, it is not difficult to maintain anesthesia by injecting 1 or 2 c.c. of the solution whenever the patient phonates or moves.

In deep anesthesia, respirations are shallow and when anesthesia is light, respirations are deep. One can be guided by the depth of respiration as to the rate of injection of the solution if it is advisable to vary the depth of anesthesia but little during the operation. When the syringe has been emptied and more pentothal sodium is required, I disconnect the syringe from the needle without removing the needle from the vein and attach another syringe containing an additional amount of solution and continue to maintain anesthesia. If the patient becomes cyanotic, no time should be lost in administering oxygen or oxygen and carbon dioxide in order to be sure of avoiding serious untoward results. When the operation is completed and the needle is withdrawn from the vein, I do not apply a dressing but simply apply mild pressure with an alcohol sponge to the site of venipuncture until hemostasis occurs. The largest doses that we have used at the clinic have been in operations on the brain. In one case a dose of 33 grains (2.2. gm.) was used and in another, 35 grains (2.3 gm.). The operation in each case lasted about three and a half hours.

The pharyngeal reflex is not greatly diminished during anesthesia with pentothal sodium, and if one wishes to use the drug for operations on the throat or for instrumentation, such as bronchoscopy, the throat should be anesthetized with a local anesthetic agent, just as if a general anesthetic agent were not to be used. When this has been done, one often finds pentothal sodium to be a suitable general anesthetic to supplement the effect of the local anesthetic. Because a collection of mucus or secretions in the throat would interfere with respiration, the administration of atropine with the preliminary medication is important in many cases. I have noticed that the urine of an ambulatory patient is highly colored following the intravenous administration of pentothal

sodium and it has an odor somewhat like the original solution of pentothal sodium.

If pentothal sodium is to be administered to ambulatory patients, the patient should be made to lie down for a sufficient period of time until he can walk without staggering. He should be accompanied to his home by some responsible person and should be treated as though he were mildly intoxicated with alcohol.

There are patients who display certain undesirable reactions to the anesthetic, such as tremor, sneezing, coughing, and hiccuping. In almost all instances these undesirable results occur in the induction period rather than in the period of maintenance. For example, sneezing, coughing, or hiccuping seldom has occurred after the administration of the first 0.5 gm. of the drug. However, if these symptoms persist beyond this point, it is probable that the patient is unsuitable for this anesthetic. In the choice of any anesthetic agent one must modify that choice according to the patient's tolerance for the agent chosen, and if the patient does not tolerate the agent well, it is wise to change to another agent or method. A respiratory stimulant may not be necessary in all cases, but as yet I have seen only a few patients who did not respond well to the combination. Picrotoxin has also been used. I add 3 mg. of the drug to each gram of pentothal sodium. It has seemed to be almost as satisfactory as has coramine. In a few cases in which 2 c.c. of metrazol was added to 1 gm. of pentothal sodium, the results were not as satisfactory as were those obtained with the other two stimulants.

INDICATIONS AND CONTRAINDICATIONS

The types of cases in which pentothal sodium has been used are indicated in Table 1. Most of the cases included in operations on the spinal cord are those in which lumbar puncture was to be done and the patient was resistant. When pentothal sodium was used to permit spinal puncture for diagnosis, the spinal fluid contained a certain amount of the drug or its decomposition products; examination of the spinal fluid, therefore, may yield interesting information. Chemical examination of the spinal fluid reveals that some of the pentothal sodium enters the spinal fluid in a few minutes after its intravenous administration. Operations on the eye included a variety of operations, particularly enucleation of the eye. Operations on the head and neck were mostly plastic operations and operations in which fireproof conditions were essential because of the use of the diathermy apparatus.

Anesthesia in cases in which individuals are resistant may be induced with pentothal sodium and supplemented with nitrous oxide and oxygen administered intratracheally, with entirely fireproof conditions. There is good control of the patient and he has the usual period of postoperative sleep. Dental extraction has been done under pentothal sodium anesthesia in a few cases in which patients demanded the anesthetic. In a few instances the intravenous method seemed to be indicated from a history of previous unsatisfactory results with both local and general anesthetic agents. The intravenous method is very popular for certain urologic cases[36] and it has almost entirely supplanted the use of gas in such cases. The two methods most frequently employed in these cases are either intravenous or spinal anesthesia. For short operations, such as manipulation of a stiff joint, changing of a cast on sensitive persons, and removal of packs and drains, this method is particularly useful.

The intravenous use of pentothal sodium seemed to be particularly valuable in certain operations on the thorax, although I advise against the use of the agent for individuals who have pulmonary disease with dyspnea. Contrary to our expectation at the clinic, the results have been rather satisfactory, no doubt because of the fact that profound anesthesia with the associated respiratory depression is not necessary for operations on the thorax. Intravenous anesthesia is also very satisfactory for

operations on the breast, particularly biopsy. Under local anesthesia most people are psychologically upset if biopsy proves that the lesion in the breast is malignant, and it may be difficult to induce general anesthesia by inhalation for radical amputation of the breast because of the excitement of the patient. In such cases the patient is usually spared this disagreeable experience if anesthesia is induced with pentothal sodium and maintained with a general inhalation anesthetic, if necessary. Anesthesia may be established in the same manner for operations on the axilla.

In some instances, usually in cases in which an appendectomy is to be performed, one may prefer to avoid the use of spinal anesthesia and to use the intravenous method. This is especially true in cases in which the patients are children who may have complicating medical conditions such as diabetes or pulmonary tuberculosis. Indications for use of the intravenous method in intra-abdominal operations are not as clear cut as they might be, except in cases in which cautery is to be used on the stump of the appendix. Operations on the abdominal wall often may be performed satisfactorily under intravenous anesthesia.

Gynecologic operations for which the drug was used were principally dilatation and curettage and examination under anesthesia. This method of anesthesia seems to be becoming increasingly popular for these procedures. Removal of painful packs and examination of the anus postoperatively constituted most of the conditions for which pentothal sodium was used in anal operations. The following case suggests another indication for use of the drug.

A woman, age thirty-three years, who was suffering from asthma following the ingestion of aspirin for which she had an idiosyncrasy and on whom a hemorrhoidectomy had been performed, was to have a pack removed. Pentothal sodium was administered intravenously and in a few moments breathing became less noisy than it had been. In a few more minutes it was free and relatively noiseless and the patient woke up without any asthmatic dyspnea. Whether or not other asthmatic patients will find some relief from this agent remains to be seen. This patient had received 65 c.c. of a 1 per cent solution of metycaine two days previously to produce sacral block for hemorrhoidectomy and there were no signs of an untoward reaction. Her preoperative medication consisted of 1/6 grain (0.01 gm.) of morphine sulphate hypodermically and 1.5 grain (0.097 gm.) of pentobarbital sodium (nembutal) by mouth.

Originally, the short acting barbiturates or those of transient effect were advocated only for short operations. More recently, the technique of intermittent administration has permitted their use in longer operations. Obviously, the patient to whom a large dose is given has a longer period of postoperative sleep than the one to whom a smaller dose has been administered. Untoward results have been few and they have occurred only when the technique here recommended was not followed. In some instances the postoperative period of sleep seemed to be beneficial. A few patients have been nauseated postoperatively and some have not enjoyed the feeling of inebriation that is experienced following the use of these agents.

I feel that there are definite contraindications to the use of the drug. In general, it should not be administered to a patient suffering from dyspnea attributable to respiratory changes or in cases in which dyspnea may develop during or after operation. This is especially true if there is any reason to think that the respiratory passage is, or may become, obstructed.

USES OF PENTOTHAL SODIUM

In some instances when pentothal sodium is administered intravenously the patient may be able to answer questions during operations with apparent honesty and yet have no memory of having talked. This seems to indicate that the drug might be useful in the interrogation of certain individuals in medicolegal practice. Two men to whom the drug was given in the Scientific Crime Detection Laboratory of

Northwestern University School of Law, with the cooperation of Leonarde Keeler, were able to answer questions either truthfully or untruthfully as they wished, even though they afterward had no recollection of what they had said or even what questions had been asked them. It is probable that pentothal sodium might find useful application in this connection, and its usefulness as a substitute for twilight sleep should be considered. As far as I know, the drug has not yet been used in obstetric practice and has not been used often as an analgesic.

When pentothal sodium is used as a prognostic agent,[2] a respiratory stimulant is not added to the anesthetic solution nor is preliminary medication administered. The results of this use of pentothal sodium have shown that it is capable of raising the temperature of the extremities to their maximal point. In cases of essential hypertension, the lowest point to which the blood pressure falls during the injection of a dose of the drug sufficient to raise the temperature of the extremities to its maximum coincides fairly well with the level of blood pressure following neurosurgical treatment in most cases.

For the average adult, 15 c.c. of a 5 per cent solution of pentothal sodium is injected in about fifteen minutes. Occasionally, the patient may require a little less or a little more of the drug. To determine the temperature of the skin during anesthesia one lead of an electric thermocouple is placed on the skin of each of two or three toes on each foot. The value for the blood pressure and the temperature of the skin are determined about every two minutes during anesthesia. Usually within fifteen minutes the temperatures of the skin of the toes have reached a maximum, but if the temperature still increases, the injection should be continued until there is no further increase. The "preoperative prediction values," then, are considered as the lowest values for the systolic and the diastolic pressures determined during the study. In vasospastic disease the affected extremity responds less than the unaffected extremity or extremities with elevation of temperature. It is probable that the rise of temperature is in reverse proportion to the pathologic changes present. The operation performed on those patients to whom it is recommended following the test is two-stage bilateral resection of the splanchnic nerves, first and second lumbar ganglions and connecting rami, and partial resection of the celiac ganglions and suprarenal glands through a modified kidney incision.[1]

A man, aged forty-three years, whose weight was 161 pounds, and whose systolic and diastolic blood pressures were 230 and 130 respectively received 1 gm. of pentothal sodium in fourteen minutes as a test for hypertension. He did not become unconscious at any time during the injection and the blood pressure was not affected by the drug. Five minutes after completion of administration of the drug the patient was wide awake. The cold pressor test has been applied in several cases following injection of a dose of pentothal sodium. In one case in which the values for the blood pressure had been lowered from 245 mm. of mercury for the systolic and 145 mm. of mercury for the diastolic to 155 mm. of mercury for the systolic and 130 mm. of mercury for the diastolic, the values returned immediately to their previous levels. The patient awoke from the effect of the anesthetic sufficiently within this short period of time to carry on a conversation.

Although one may expect the blood pressure to fall when pentothal sodium is administered intravenously, in a few surgical cases I have seen it rise so that there was a definitely undesirable effect. In one instance the operation involved the brain and under those circumstances this action was particularly undesirable. I recall a similar situation that occurred several years ago in connection with intravenous anesthesia with sodium amytal. The blood pressure rose and remained so high that it was necessary to discontinue the opera-

tion. There is some uncertainty in my mind as to the significance of the various factors involved. Recently, in an operation on the brain, anesthesia was induced with ether. The blood pressure rose to an alarming level and remained high for a time while the surgeon delayed operation to make certain that it would be safe to proceed. At his suggestion pentothal sodium was administered and the administration of ether was discontinued. In a few moments the patient's blood pressure began to fall and in a short time it was at a relatively normal level. The operative procedures were instituted and after the 1 gm. of pentothal sodium had been administered, ether anesthesia was resumed without further untoward results.

The values for blood sugar and blood urea were determined in a representative group of cases by Betlach and Tovell.[3] They found that the concentration of blood sugar is raised appreciably by pentothal sodium, as it is by other derivatives of barbituric acid. However, the difficulty of controlling the metabolism of carbohydrate in cases of diabetes in which the drug has been administered has not been increased materially. The variation in the concentration of blood urea before and after anesthesia was negligible.

In emergency, an immediately available solution of pentothal sodium might be lifesaving.* Because pentothal sodium injected intravenously would be the treatment for ether convulsions it probably ought to be readily available at all times in the operating room where general anesthetics are being administered.

COMMENT

Although evipal soluble and pentothal sodium seem to be the best agents available for intravenous anesthesia, it is probable that other agents will be developed which may be better. As yet it is undesirable for the inexperienced person to use these drugs, for it is as true of these agents as it is of other anesthetic agents, that the results obtained depend largely on the skill and caution with which the agent is administered and on a good understanding of its applicability.

* I have been able to demonstrate the value of having a solution of pentothal sodium immediately available in the syringe in the case of a woman who had taken a dose of cocaine between 0.5 to 1 gm. and convulsions had begun. The pentothal sodium was administered immediately by vein and the convulsions stopped.

REFERENCES

1. Adson, A. W., Craig, W. McK. and Brown, G. E. Surgery in its relation to hypertension. *Surg., Gynec., and Obst.*, 62: 314–331 (Feb. 15) 1936.
2. Allen, E. V., Lundy, J. S. and Adson, A. W. Preoperative prediction of effects on blood pressure of neurosurgical treatment of hypertension. *Proc. Staff Meet. Mayo Clin.*, 11: 401–406 (June 24) 1936.
3. Betlach, C. J. and Tovell, R. M. Blood sugar and blood urea determinations before and after anesthesia with pentothal sodium. Unpublished data.
4. Bosse, P. Ueber intravenöse Pernoktonnarkose. *Deutsch. med. Wbnschr.*, 54: 272–273 (Feb. 17) 1928.
5. Bumm, R. Intravenöse Narkosen mit Barbitursäurederivaten. *Klin. Wchnschr.*, 6: 725–726 (April 16) 1927.
6. Burkhardt, Ludwig. Die intravenöse Narkose mit Aether und Chloroform. *München. med. Wchnschr.*, 56: 2365–2369 (Nov. 16) 1909.
7. Cleisz, Louis. L'anesthésie obstétricale par injection intraveineuse de somnifène. A propos de 40 nouvelles observations. *Presse méd.*, 32: 1001–1005 (Dec. 17) 1924.
8. Constantin, J. D. General anesthesia by the intravenous injection of ethyl alcohol. *Lancet*, 1: 1247 (June 15) 1929.
9. Constantin, J. D. General anesthesia by the intravenous injection of ethyl alcohol. *Lancet*, 1: 1393–1395 (June 28) 1930.
10. Döring, Oskar. Erfahrungen über die intravenöse Narkose mit Eunarcon (R. 1238). *Deutsch. med. Wchnschr.*, 61: 868–871 (May 31) 1935.
11. Dreser. Ueber ein neues Hypnoticum aus der Reihe der Urethane. *München. med. Wchnschr.*, 46: 1310 (Oct. 3) 1899.
12. Fredet, Pierre and Perlis, Régine. Recherches sur un nouveau mode d'anesthésie generale. *Bull. et mém. Soc. nat. d. chir.*, 50: 789–802 (June 25) 1924.
13. Graet, Wilhelm. Bericht über Erfahrungen mit den intravenösen Aether- und Isopral- Aether-Narkosen. *Beitr. z. klin. Chir.*, 83: 173–211 (Feb.) 1913.
14. Heard, K. M. Pentothal: a new intravenous anaesthetic. *Can. Med. Assn. Jour.*, 34: 628–634 (June) 1936.
15. Jackson, D. E. and Lurie, L. A. Experimental and clinical observations on the actions and therapeutic uses of ethylisopropylbarbituric acid. *Jour. Lab. and Clin. Med.*, 11: 116–122 (Nov.) 1925.

16. Jarman, Ronald and Abel, A. L. Intravenous anaesthesia with pentothal sodium. *Lancet*, 1: 422–423 (Feb. 22) 1936.
17. Jarman, Ronald and Abel, A. L. Technique of intravenous anaesthesia. *Lancet*, 1: 600 (March 14) 1936.
18. Keller, O. Numal anesthesia. *Ugesk. f. Laeger.*, 89: 254 (March 31) 1927.
19. Kirschner, M. Eine psycheschonende und steuerbare Form der Allgemeinbetäubung. *Cbirurg.*, 1: 673–682 (June 15) 1929.
20. Krawkow, N. P. Ueber die Hedonal-Chloroform-Narkose. *Arcb. f. exper. Patb. u. Pharmakol.* (Suppl.), 317–326, 1908.
21. Lundy, J. S. The barbiturates as anesthetics, hypnotics and antispasmodics: their use in 1000 surgical and nonsurgical cases in man and in operations on animals. *Proc. First Pan-Pacific Surg. Conf., Honolulu* (Aug. 14–24) 1929.
22. Lundy, J. S. Intravenous anesthesia: particularly hypnotic, anesthetic and toxic effects of certain new derivatives of barbituric acid. *Current Res. Anestb. and Anal.*, 9: 210–217 (Sept.-Oct.) 1930.
23. Lundy, J. S. Intravenous anesthesia: preliminary report of the use of two new thiobarbiturates. *Proc. Staff Meet. Mayo Clinic*, 10: 536–543 (Aug. 21) 1935.
24. Lundy, J. S. A method of minimizing respiratory depression when using soluble barbiturates intravenously. *Proc. Staff Meet. Mayo Clinic*, 10: 791–792 (Dec. 11) 1935.
25. Lundy, J. S. and Tovell, R. M. Some of the newer local and general anesthetic agents: methods of their administration. *Northwest Med.*, 33: 308–311 (Sept.) 1934.
26. Lundy, J. S. and Tovell, R. M. Annual report for 1934 of the Section on Anesthesia: including data on blood transfusion. *Proc. Staff Meet. Mayo Clinic*, 10: 257–272 (April 24) 1935.
27. Lundy, J. S., Tovell, R. M. and Tuohy, E. B. Annual report for 1935 of the Section on Anesthesia: including data on blood transfusion. *Proc. Staff Meet. Mayo Clinic*, 11: 421–432 (July 1) 1936.
28. Magill, I. W. Anaesthesia in thoracic surgery, with special reference to lobectomy. *Proc. Roy. Soc. Med.*, 29: 643–652 (April) 1936.
29. Marin, M. G. Quoted by Constantin, J. D.[8]
30. Noel, H. and Souttar, H. S. The anesthetic effects of the intravenous injection of paraldehyde. *Ann. Surg.*, 57: 64–67 (Jan.) 1913.
31. Oré, L. Nouvelle note sur les injections intraveineuses de chloral. *Bull. Soc. de cbir. de Par.* (1872), s. 3, 1: 350, 400, 1873.
32. Peck, C. H. and Meltzer, S. J. Anesthesia in human beings by intravenous injection of magnesium sulphate. *Jour. Am. Med. Assn.*, 67: 1131–1133 (Oct. 14) 1916.
33. Petit, Gabriel and Perlis, Régine. Anesthésie du chien par l'allyl-isopropyl-barbiturate de diéthylamine. *Compt. rend. Soc. de biol.*, 94: 978–979 (April 17) 1926.
34. Pratt, T. W., Tatum, A. L., Hathaway, H. R. and Waters, R. M. Sodium ethyl (l-methyl butyl) thiobarbiturate: preliminary and experimental clinical study. *Am. Jour. Surg.*, 31: 464–466 (March) 1936.
35. Sweebe, E. E. and Khuen, E. C. Pentothal sodium (thiobarbiturate No. 8064), a new anesthetic. *North Am. Vet.*, 17: 31–33 (Jan.) 1936.
36. Thalheimer, Marcel. Anesthesia by intravenous injection of 1-methyl-5, 5-allyl-isopropyl-barbituric acid. (In press.)
37. Tovell, R. M. and Thompson, G. J. Pentothal sodium anesthesia in urologic practice. *Jour. Urol.*, 36: 81–87 (July) 1936.
38. Weese, H. and Scharpff, W. Evipan, ein neuartiges Einschlafmittel. *Deutscb. med. Wcbnscbr.*, 58: 1205–1207 (July 29) 1932.
39. Zerfas, L. G., McCallum, J. T. C., Shonle, H. A., Swanson, E. E., Scott, J. P. and Clowes, G. H. A. Induction of anesthesia in man by intravenous injection of sodium iso-amyl-ethyl barbiturate. *Proc. Soc. Exper. Biol. and Med.*, 26: 399–403 (Feb.) 1929.

THE PROTECTIVE ACTION OF PICROTOXIN IN PROLONGED SURGICAL ANESTHESIA WITH EVIPAL*

A. H. MALONEY, PH.D., M.D.

Professor and Head, Department of Pharmacology and Consultant in Pharmacology at Freedmen's Hospital

WASHINGTON, D. C.

EVIPAL soluble, the sodium salt of n-methyl-cyclohexenyl-methyl malonyl urea, is one of the newer barbiturates characterized by a powerful hypnotic and anesthetic index associated with a remarkably rapid rate of destruction in the system when administered parenterally. This latter characteristic accounts for its rather low toxicity as compared with other short acting barbiturates like nembutal, pernocton and phanodorn.

With respect to its therapeutic index Killian[1] reported a toxic-narcotic ratio of 100:24–27 in rabbits; Weese[2] a toxic-narcotic ratio of 100:25 in cats and 100:30 in dogs; Kennedy[3] a toxic-anesthetic ratio of 100:25–32 intraperitoneally in mice and rats; Maloney and Hertz[4] a toxic-anesthetic-hypnotic ratio of 100:36:18 in rats and approximately 100:24:20 in rabbits, both intraperitoneally; Gwathmey[5] a toxic-anesthetic ratio of 100:33, intraperitoneally, in dogs, and Storm[6] a toxic-narcotic ratio of 100:15, intraperitoneally, in monkeys.

With respect to its destruction Killian[1] has found that the rabbit detoxifies twice the minimal narcotic dose in thirteen minutes, while Halberkann[7] has indicated that evipal, in contradistinction to other barbiturates, is almost wholly destroyed (97 per cent) in the organism. He was able to recover only 2.8 per cent (average) in the urine of dogs. In the rapidity with which it is disposed by the body evipal bears close resemblance to the gaseous anesthetics, state Coryllos and Bass.[8] In the speed of its dynamic effects it surpasses them.

Here is an anesthetic agent exhibiting a remarkable pharmacodynamic activity which is so quickly detoxified by the defense mechanisms of the body that, with due care as to the rate of injection, several doses far in excess of the safety expectancy of a single injection may be successfully employed. In a previous report on this study Maloney and Hertz[4] recorded this pertinent observation:

> The hazard of toxicity is inherent not in the drug per se but rather in its absorption constant in the system in any unit of time. The detoxifying mechanism can cope adequately with a vast quantity of the compound spread over a relatively long period of time whereas it may easily be overwhelmed by a mere fraction of that same amount if absorbed in a moment. . . . Safety and therapeutic efficiency are consequently functions of rate and degree of absorption.

Having had considerable laboratory experience with picrotoxin administered before, combined with, and following the administration of lethal doses of other barbiturates, we treated a case of respiratory embarrassment which occurred early in the course of our animal experimentation with evipal in prolonged anesthesia. The counteracting action of picrotoxin in this case was so effective that it suggested the feasibility of the employment of picrotoxin as a routine prophylactic measure.[9] Using this technique in numerous laboratory experiments the fact was established that whereas picrotoxin has no inhibitory or retarding effect on the anesthetic action of evipal it effectively prevents the possibility of respiratory paralysis. Since the danger in the intravenous administration of evipal for purposes of anesthesia lies in its possible assault on the respiratory center it follows

* From the Department of Pharmacology, Howard University School of Medicine and Freedmen's Hospital, Washington, D. C.

logically that the antecedent protection of this center against such impending assault is good pharmacological procedure. Picrotoxin provides this protection. Consequently all our clinical cases on whom evipal is used for prolonged anesthesia receive routinely a prophylactic dose of picrotoxin.

TECHNIQUE

Selection of Patient. Since evipal is detoxified principally, if not entirely, by the liver we consider functional impairment of this organ the major contraindication. Accordingly, a negative Fouchet test is done routinely before evipal is selected as the anesthetizing agent. In the series of cases here reported (Table 1) no other condition presented itself either as a contraindication or complication following its use. Mention of other possibilities will be made in the discussion.

Preparation of Patient. The patient is prepared in the usual manner. When necessary psychic or nervous stabilization on the night preceding the operation is obtained by the use of morphine-scopolamine, but under no circumstances is preanesthetic medication allowed. Preliminary sedation both complicates the general picture and prevents a correct estimation of the effective anesthetizing dose of evipal. On this matter we are in accord with Heard[10] and Killian.[1] Heard says that preoperative sedatives should be used with caution; and Killian says that their use with evipal is not recommended since their depressant action combines with the action of evipal and impairs respiration.

Induction. Upon signal of readiness from the surgeon 2 c.c. of a 0.3 per cent solution of picrotoxin is injected intramuscularly, the deltoideus being the site usually selected. This is followed by an immediate enhancement of the rate and (or) depth of respiration. The patient is then asked to count audibly as soon as the needle delivering the evipal solution has been inserted into the vein and the injection has begun. The injection is made fairly rapidly until the patient's voice fades away. An additional one-third of the dose already delivered is then given and the injection is stopped, the needle being held in the vein. The signal is now given the surgeon to begin. Using the same calibre syringe and needle at all times the technician quickly learns to gauge the optimal rate of injection. Individual variations become a negligible factor with the rapidly acquired experience. Because of the relative length of the systemic circulation in man as compared with small laboratory animals the rate of injection in man has to be correspondingly increased in order to produce anesthesia, so rapidly is the drug detoxified. Undue slowness of injection rate serves to retard the induction time as well as boost the initial amount of the anesthetic. The average induction time is twenty to thirty seconds. The presence of picrotoxin in the system acts as a virtual buffer against untoward embarrassment. Respiratory accidents are reduced to the vanishing point with the employment of this technique.

ANALYSIS OF CASES

Blood Pressure. The blood pressure is recorded prior to the administration of picrotoxin. Whenever possible the sphygmomanometer is kept on the arm in which event the pressure is recorded at intervals of five minutes throughout the operation. In every case the pulse and respiration rates are taken at five minute intervals. There is usually an insignificant initial fall of pressure, but this tends to right itself. In our cases the drop was merely 2 to 10 mm. In 2 instances an actual rise in the systolic pressure occurred (150 to 170 and 126 to 130). Two cases exhibiting hypertension showed marked drops (240 to 200 and 160 to 88). In one patient, twenty-five years of age, a pressure of 138 dropped to 92. The average systolic pressures at the beginning and end of the operation for the series were 133 mm. and 118 mm. respectively, constituting an average fall of approximately 15 mm. We have taken a

fall of 30 mm. in an initially normal pressure reading as one indication for a supportive dose of picrotoxin.

Pulse. As a rule the pulse rate tends to increase during the course of the operation. Ten cases in our series manifested slight decreases comparing the rates at the end with those at the beginning. The average pulse rates per minute at the beginning and end were 105 and 116 (10 per cent). Changes in the rate are of minor significance as compared with associated changes in the quality of the pulse. Any sign of threadiness or weakening in the course of an operation is construed as another indication for a supportive dose of picrotoxin.

Respiration. The rate of respiration also tends to increase but like the pulse the increase is not marked. Five showed slight decreases (26–24, 24–18, 36–25, 40–32, 48–40). Three showed considerable increases at the end over the initial rate (22–56, 20–68, 22–68). The majority (78 per cent) showed slight increases. The average increase was 8 per minute, from 29 at the beginning to 37 at the end of operation.

Under evipal anesthesia the respiration closely simulates physiological sleep usually exhibiting a gentle stertor with a definite rhythmicity and depth. We take the quality of the respiration as our cardinal sign, either withholding the evipal administration or gauging the fractional doses according to the minutest detectable changes of rhythm or depth. In this way a smooth course of anesthesia is maintained. Our fractional doses, therefore, are characterized more by smallness and frequency than by quantity. In this connection it is pertinent to state that impairment of rhythm and depth may result from obstruction of the air passage. Unless it causes gagging the mechanical Cornell airway is used routinely. We have had no cases in which apnea, hyperpnea, asphyxia or shock was observed, or anxiety exhibited by surgeon or anesthetist. In no case did any untoward condition arise remotely suggesting an emergency calling for the use of oxygen-carbon dioxide or any other respiratory stimulant.

Quality of Anesthesia and Relaxation. Care was taken after each operation to have the surgeon express in writing his impressions regarding the quality of the anesthesia and the nature of the relaxation of skeletal muscle and abdominal viscera. These impressions are recorded in the table.

Postoperative Notations. The records reveal one case developing "pleuritic pains" on the fourth postoperative day and one a "hypostatic or bronchial pneumonia" on the second day. Both cases cleared following digitalis medication. The anesthetic, in our opinion, had no causal connection with either condition. There have been no instances of postoperative gastric distress, intestinal distention or malaise. The strict withholding of fermentable or gas-producing foods and drinks may probably have played a beneficial role. The most clamant postoperative disturbance in our records is what is variously described as restlessness, irritability, hyperexcitability, and tremors. For the first case where restlessness was observed postoperatively 180 mgm. of nembutal was ordered, as we felt that the restlessness was probably due to some residue of picrotoxin in the system. However, with notices in the literature (*c.f.* Heard,[10] Coryllos and Bass,[8] et al.) of such a condition obtaining in which no analeptic was administered it was suspected that the anesthetic agent might play some role in the production of this hypersensitiveness. We tried morphine with unvaryingly good results. A single dose of morphine, 10 or 15 mgm., with or without atropine has always given the desired sedation; (see also Heard[10]).

Of the 40 cases presented in this report 26 or 65 per cent lasted fifty minutes or more from the time of incision to the making of the last suture. Of these 26, 18 occupied sixty minutes or more and of the 18, 3 lasted 133, 125 and 125 minutes respectively; the average duration for the series was 58.85 minutes. The average dose per person of evipal used throughout the

No.	Patient			Operation	Duration Minutes	*Total Evipal Grams	Blood Pressure		Picrotoxin during Operation	Respiration			Pulse		Surgeon's Comments	Postoperative Observations of the Internes
	Sex	Age	Weight				Start	End		Start	End	Quality	Start	End		
March, 1936																
1	F	27	165	Cesarean; sterilization; Wassermann 4+	64	2^{10}	240/148	200/140	6 mgm.	40	48	regular	96	132	"Gut is just as relaxed as in spinal anesthesia" J. W. Ross	Restless—nembutal 180 mgm.; uneventful recovery
2	F	21	115	Cesarean section with sterilization	50	2.6^{8}	120/80	112/80	None	32	40	regular	110	144	"Anesthesia and relaxation good" J. W. Ross	500 c.c. 5 per cent glucose during operation, 1000 c.c. 10 per cent glucose after operation; good recovery; discharged sixteenth postoperative day
3	F	40	210	Cesarean section; sterilization; para 11, placenta previa	60	2^{7}	130/80	120/80	12 mgm.	44	..	regular	120	120	"Good relaxation" J. W. Ross	Restless on awakening; morphine 15 mgm.; uneventful recovery
4	F	21	138	Cesarean section	50	2.6^{10}	114/66	.....	None	..	..	.....	...	...	"Silent abdomen" J. W. Ross	Uneventful recovery
5	F	40	165	Sterilization—para 13, glomerulonephritis	40	1.6^{6}	180/100	166/94	None	22	56	jerky—regular	84	112	"Gut as silent as with spinal anesthesia" J. W. Ross	Slight restlessness; uneventful recovery
6	F	23	135	Cesarean section	47	2^{11}	140/90	130/90	None	30	30	regular	120	108	"Anesthesia excellent" J. W. Ross	Very restless; morphine 15 mgm., recovery uneventful
7	F	20	124	Excision of hip joint, tuberculosis of hip	63	1.6^{8}	118/60	116/68	None	20	28	regular	148	114	"Quality perfect; relaxation fair" P. T. Johnson	Recovery uneventful
April, 1936																
8	F	53	145	Open reduction of fracture of humerus	69	1.5^{6}	Not taken	.....	None	26	24	regular	120	125	"Quality and relaxation good" P. T. Johnson	Quiet; uneventful
9	F	24	115	Cesarean section with sterilization	91	2.4^{14}	130/80	100/70	None	45	48	regular	100	120	"Anesthesia gave good relaxation of intestines and abdominal muscles" J. W. Ross	Very restless 7 hours postoperatively; morphine 15 mgm. with atropine 0.5 mgm.
10	M	39	165	Open reduction right tibia; intramedullary graft	87	2.1^{9}	130/80	116/78	6 mgm.	36	25	regular	120	72	"Relaxation good; quality good" P. T. Johnson	Quiet; uneventful recovery
11	M	26	160	Comminuted intercondylar fracture of right humerus	67	2.1^{10}	128/80	.....	None	30	30	regular	84	72	"Relaxation very good" P. T. Johnson	Quiet; uneventful recovery
12	F	43	120	Appendectomy	28	1^{1}	130/80	120/75	None	22	24	regular	116	94	"Complete relaxation of abdominal wall; intestines very quiet. The anesthesia was perfect" H. R. Burwell	Pleuritic pains on fourth day; cleared up with digitalis. Recovery complete, uneventful

13	F	38	150	Appendectomy; multiple myomectomy; right salpingectomy, left plastic	133	4.7[10]	130/76	104/66	None	20	40	regular	112	120	"Relaxation good; smooth anesthesia throughout" J. W. Ross	Respiration shallow, heart rate 107, weak; sleep profound. Picrotoxin 6 mgm. Restless after fifth hour. Morphine 15 mgm. Recovery complete
14	M	20	175	Appendectomy	43	1.6[5]	110/64	100/66	3 mgm.	18	28	regular	112	128	"Relaxation very good" W. M. Lane	No postoperative distention; no excitement
15	F	14	112	Appendectomy	39	1[5]	116/80	110/70	None	28	38	fairly regular	120	136	"Relaxation immediate; best towards last part of operation" W. M. Lane	No postoperative disturbance. Recovery uneventful
16	F	34	112	Right mastoidectomy	24	1[5]	115/80	110/70	None	24	18	regular	116	120	"Anesthesia very good; no sign of shock" H. W. Barnes	No postoperative ill effects; no irritability
17	F	25	114	Appendectomy, ovarian cyst, right	32	1.1[3]	138/60	92/62	3 mgm.	20	20	regular	82	120	"Relaxation complete six minutes after the beginning of anesthesia" W. H. Welch	No sign of irritability; no postoperative discomfort
18	F	47	180	Herniorrhaphy	60	1.4[7]	164/100	154/100	None	18	20	regular	60	84	"The gut is just as flat as in spinal anesthesia" A. M. Curtis	Developed hypostatic or bronchial pneumonia second day postoperative. Digitalis and morphine cleared it up in three days. Good healing
19	M	20	165	Appendectomy	50	1.6[7]	130/76	120/70	None	20	20	regular	78	84	"In the first part of operation intestines were pushed out because of impaired respiration. Tongue had occluded the respiratory passage. After tongue was pulled out relaxation was complete" W. M. Lane	Postoperatively patient is in excellent condition
20	F	16	115	Laparotomy; exploratory	42	1.3[5]	123/80	98/60	None	44	40	regular	96	108	"Relaxation good; quality of anesthesia good" H. R. Burwell	Very restless; morphine 15 mgm. atropine 1 mg. No vomiting; no distention; no complications
21	F	18	136	Appendectomy	55	1.8[11]	78/58	68/50	None	40	48	regular	118	120	"Excellent anesthesia" H. R. Burwell	Somewhat irritable; no vomiting; good postoperative condition
22	F	28	118	Laparotomy	70	1.5[5]	160/100	88/72	3 mgm.	30	30	regular	84	60	"Good relaxation throughout; very good anesthesia" H. R. Burwell	No postoperative disturbances. Recovery complete
23	F	34	125	Dilatation of rectal stricture; lymphogranuloma inguinale	30	1.3[6]	138/90	110/74	None	32	32	regular	120	120	"Relaxation splendid; quality of anesthesia excellent" F. Jones	No postoperative disturbance. Good condition throughout convalescence

* Small figure represents number of fractional injections.

No.	Patient			Operation	Duration Minutes	*Total Evipal Grams	Blood Pressure		Picrotoxin during Operation	Respiration			Pulse		Surgeon's Comments	Postoperative Observations of the Internes
	Sex	Age	Weight				Start	End		Start	End	Quality	Start	End		
April, 1936																
24	F	39	180	Appendectomy; dermoid cyst in abdominal cavity	60	1.7[5]	150/90	102/50	None	44	48	regular	112	128	"Anesthesia most satisfactory" H. R. Burwell	Hyperexcitable; morphine and atropine; abdominal distention for two days but no other complication
May, 1936																
25	F	25	180	Appendectomy, right salpingo-oophorectomy, left partial salpingo-oophorectomy	71	1.9[6]	148/68	130/68	None	24	40	regular	96	136	"Relaxation good" H. R. Burwell	Slightly restless. Recovery uneventful
26	F	20	110	Appendectomy	39	2[8]	112/78	98/72	None	36	36	regular	160	108	"Anesthesia entirely satisfactory; relaxation perfect" W. H. Welch	No postoperative discomfort
27	F	20	120	Decompression; fracture of left temporal region	45	2.2[7]	110/68	110/70	None	26	40	regular	120	150	"This anesthetic seems to be ideal for this type of operation" A. M. Curtis	Condition good; recovery uneventful
28	F	28	118	Appendectomy, bilateral oophorectomy	60	2[4]	130/83	108/78	None	40	40	regular	150	140	"Good relaxation" W. H. Welch	No postoperative discomfort, rapid convalescence
29	F	24	120	Lymphogranuloma inguinale	17	1.3[3]	150/100	170/110	None	48	40	regular	108	164	"Relaxation good for 15 minutes" H. R. Burwell	Patient comfortable. No postoperative disturbance
30	F	23	138	Bilateral salpingectomy; appendectomy; freeing adhesions	50	2.1[8]	110/90	100/78	None	22	30	regular	84	120	"Anesthesia fine" W. H. Welch	No postoperative disturbance. Condition satisfactory during convalescence
31	F	33	180	Cesarean section with sterilization	78	1.8[9]	126/80	130/110	None	24	40	Apneic to begin, later regular	88	120	"Relaxation adequate" J. W. Ross	Came out of anesthesia without restlessness; was unable to void urine eighteen hours postoperative; catheterized; recovery uneventful
32	M	37	160	Amputation of penis by electrocautery	28	1.8[5]	162/92	150/100	None	40	32	regular	84	120	"Good relaxation; good anesthesia" R. F. Jones	No signs of irritability; no vomiting, gradual convalescing uneventful recovery
June, 1936																
33	F	42	100	Appendectomy; supravaginal hysterectomy; bilateral salpingo-oophorectomy	53	1.6[6]	160/110	140/110	3 mgm.	20	68	irregular, jerky and shallow	120	140	"Abdominal wall and intestines well relaxed. Anesthesia very satisfactory. (R. L. Jackson Provident Hospital, Baltimore, Md.)"	Patient awoke perfectly quiet. Recovery uneventful

34	F	29	130	Appendectomy; bilateral salpingectomy; bilateral partial oophorectomy, myomectomy	125	3.0[13]	122/98	120/80	None	44	58	regular	124	116	"Very good relaxation" J. W. Ross	Postanesthetic recovery was good. Restless four hours later. From this point postoperative course was uneventful
35	F	47	...	Appendectomy; bilateral oophorectomy; hysterectomy	125	3.0[10]	138/88	120/180	None	22	68	regular	90	100	"Excellent relaxation smooth anesthesia throughout" J. W. Ross	Postanesthetic recovery good. No restlessness. Uneventful recovery
								July, 1936									
36	M	32	150	Appendectomy	44	1.2[2]	120/70	112/74	None	16	32	regular	80	120	"Relaxation good" W. H. Welch	Hyperexcitable; morphine; patient states anesthesia was very good, prefers it to ether
37	F	27	147	Dilatation of rectal stricture	95	1.3[4]	120/80	112/76	None	16	28	regular	84	120	"Anesthesia good; relaxation excellent" H. R. Burwell	Patient improved progressively. No adverse signs
								August, 1936									
38	F	29	108	Appendectomy, cervical dilatation curettage; left salpingectomy	50	2.8[8]	106/62	104/54	None	44	60	regular	90	110	"Perfect relaxation was gotten from anesthesia" (Mercy Hospital, Philadelphia, Pa.) Dr. Fortune	Postoperative excitement was observed. Quieted with morphine 15 mgm. Recovery uneventful
39	M	11	86	Gastrectomy	55	1.0[2]	108/75	108/72	None	16	36	regular	80	120	"Excellent relaxation" E. Howes	Patient has not experienced vomiting nor a turn for the worse since operation
								September, 1936									
40	F	34	135	Repair of vesicovaginal fistula	65	2.6[6]	140/80	112/64	None	28	28	regular	120	100	"Anesthesia all to be desired" J. W. Ross	Slightly restless; morphine 10 mgm.; made uneventful recovery

* Small figure represents number of fractional injections.

series was 1.875 gm. The largest dose used in a single case was 4.7 gm. distributed over ten fractional injections, the initial induction dose being 1 gm. Reference to the table will show the variety of operations performed.

DISCUSSION

Because of its rapid destruction in the system the adaptability of evipal for anesthesias of long duration making use of the technique of fractional injections p.r.n. was soon discovered and adopted.

Rogotzky[11] states that it is apparently harmless and especially valuable in general anesthesia of long duration. Sailer[12] and Kohlhage[13] while especially advocating its use both as a basal anesthetic and as a general anesthetic for short operations also state that it may be used for prolonged major operations. Sailer warns of the danger of the facile overdose and insists that expert induction is as necessary as in the case of inhalation anesthesia. Garrey and Cohn[14] advise the restriction of its use to good surgical risks until it has been more widely used and better understood. Cousineau[15] urges that the dosage and the rate of injections should be carefully watched. Kaminiker and Rintelen[16] report that while it is employed at the Graz Clinic for certain major operations calling for fractional injections, its employment for orthopedic operations was not approved because of the frequent occurrence of motor unrest. Beck[17] and Baetzner[18] encountered some trembling and twitching. The former attributed this to rapidity of injections, the latter to high basal metabolism which destroyed the substance so rapidly that inadequate dosage probably evoked excitation rather than sleep. He employed supportive amounts of ether or ethyl chloride in those cases. Burkle de la Camp[19] used it for basal, short and long anesthesias without any immediate deleterious results or sequela. Ernst[20] reports that prolonged anesthesia was obtained by fractional doses but advises against this because of frequent changes in the depth of narcosis which is a disadvantage alike to surgeon and patient.

By the prophylactic employment of picrotoxin, the incidence of respiratory embarrassment is effectively offset and by the frequency of administration of minute fractional doses the desired depth and smoothness of anesthesia is easily maintained.

Following the recommendation set forth by the manufacturers of evipal that the dosage should be gauged on the basis of 0.06 c.c. of a 10 per cent solution per pound of body weight with a maximum of 10 c.c. (1 gm.) per person, the earlier investigators tried to establish a dosimetric scale for general use. Heard[10] states that the sleep inducing dose should be one-half the full estimated weight dose. Garrey and Cohn[14] inject 3 to 4 c.c. at the rate of 1 c.c. per fifteen seconds leaving the needle in the vein for subsequent injections p.r.n. To produce anesthesia Sailer[12] injects 7 to 10 c.c. delivering the first 4 c.c. in one minute. To prolong anesthesia two-third to one-half of the initial anesthetizing dose is given. These rules are, however, only of suggestive value. Questions of idiosyncrasies, age, nutritional state, nervous set are always obtrusive. Gorodner[21] advises that nervous patients require larger and debilitated patients relatively smaller doses. Cousineau[15] reports one death occurring two minutes after the injection of 7 c.c. Morl[22] reports a case of death in three minutes of a man seventy-five years of age who received 8 c.c. and Kaminiker and Rintelen[16] report 2 cases of women, seventy years old, who manifested severe respiratory and circulatory disturbances following the injection of 7 c.c. each. Both died; one within nine hours and the other three days. Morl used his observation to stress the warning that schematic dosage according to body weight may result in overdosage. Kaminiker and Rintelen believe that their deaths were not due directly to the narcotic. Harms[23] advises that the calculated weight dosage should be checked by observation of objective symptoms during injection so as

to control factors of possible idiosyncrasies. Westerborn[24] states that young patients often needed twice as much as patients between sixty and eighty years of age and robust patients generally required more than anemic or debilitated ones. In our experience the method of individualizing our patients, using the abolition of speech as guide, has proved quite satisfactory. Its utter simplicity commends it. We are not in position to say whether or not this simple method would work satisfactorily without the prophylactic use of picrotoxin.

On the question of contraindications to the use of evipal there is a unanimity of opinion amongst investigators that hepatic dysfunction definitely contraindicates the employment of this agent. Either by way of elucidation or addition, mention has been made of marked sepsis by Merritt;[25] peritonitis by Kohlhage;[13] bronchial asthma by Boden;[26] cachexia, dehydration and certain nose and throat operations by Suraci;[27] impaired respiration and suburemic states, by Killian.[1] Early bronchiectasis, diabetes, hypertension, endocarditis and advanced carcinoma are mentioned by Heard[10] as complicating factors. Coryllos and Bass[8] present a comprehensive statement on contraindications with which we are in complete accord. They state: "It is (therefore) obvious that morbid conditions causing impairment of hepatic functions constitute formal contraindications to the use of evipal. Such conditions are jaundice —whatever the cause, acute toxemias and bacteremias, or chronic and prolonged suppurations."

SUMMARY

The adaptability of evipal soluble by fractional injections for use in prolonged clinical surgical anesthesia because of its rapidity of action and detoxification is discussed.

The efficacy of picrotoxin as a prophylactic measure to protect the respiratory center from untoward or undue assault by the barbiturate is advanced.

The technique employed in the production and maintenance of good clinica surgical anesthesia is described.

Analysis is made, and a table presented, of 40 operations performed under prolonged evipal anesthesia by the employment of this technique.

A brief discussion of the literature pertinent to the subject is presented (a) on the experiences and impressions of investigators (b) on the problem of schematic dosage and gradation of fractional doses and (c) on the question of contraindications to the use of evipal.

We wish to acknowledge with thanks our deep appreciation of the kindness of the following: The Research Department of the Winthrop Chemical Company for generously providing the evipal soluble used in this study; the surgeons whose names appear in the table for faith in our judgment; and the internes, Doctors J. C. Oliver, U. I. Carrington and T. C. Simmons for invaluable aid in the course of administering the anesthetic and for keeping the postoperative records on the condition and progress of the patients.

REFERENCES

1. Killian, Hans. The new German evipan-sodium anesthesia. *Anestb. and Analg.*, 13: 227, 1934; cf. *S.A.B.*, 7, A-1143, 1934.
2. Weese, H. Pharmacology of the intravenous short narcotic sodium evipal. *Deutscbe. med. Wcbnscbr.*, 59: 47, 1933.
3. Kennedy, Walter. Sodium salt of c-c-cyclohexenylmethyl-n-methyl barbituric acid (evipan) anesthesia in laboratory animals. *Jour. Pbarmacol. and Exper. Tberap.*, 50: 347, 1934.
4. Maloney, A. H. and Hertz, R. Sodium n-methyl-cyclohexenyl-methyl-barbituric acid (evipal): hypnosis, anesthesia and toxicity. *Jour. Pbarmacol. and Exper. Tberap.*, 54: 1, 1935.
5. Gwathmey, James T. Rectal administration of evipal soluble. *Am. Jour. Surg.*, 32: 3, 1936.
6. Storm, C. J. Pharmacological study of sodium evipan narcosis in monkeys. *Arcb. internat. Pbarmacodynamie*, 52: 97, 1935.
7. Halberkann, Von. The elimination of evipal in the urine. *Biologiscbe Abteilung*, Arztlicher Verein Hamburg, 14: 1933.
8. Coryllos, P. N. and Bass, S. Evipal anesthesia in thoracoplasties. *Anestb. and Analg.*, 15: 66 (March-April) 1936.
9. Maloney, A. H. and Hertz, R. Experiments with evipal in prolonged anesthesia. *Jour. Lab. and Clin. Med.*, 20: 12, 1935.
10. Heard, Kenneth. Clinical observations on the use of evipan. *Can. Med. Assn. Jour.*, 31: 617, 1934.

11. Rogotzky, O. Experiences with evipan-sodium as a useful intravenous anesthetic. *Therap. d. Gegenw*, 1933; through *Deutsch. med. Wchnschr.*, 59: 1061, 1933.
12. Sailer, Karl V. Evipan-sodium anesthesia in major surgery. *Klin. Wchnschr.*, 13: 305, 1934.
13. Kohlhage, T. Experience with evipan narcosis. Duisburger Aerzteverein, meeting (11/3/33); through *Münch. Med. Wchnschr.*, 81: 110, 1934.
14. Garrey, Walter E. and Cohn, Roy B. The use of sodium evipan as an anesthetic for short surgical procedures. *New England Jour. Med.*, 213: 301, 1935.
15. Cousineau, Georges. Preliminary considerations on a new intravenous anesthesia: evipan, 100 cases. *Bull. Assn. Medicins de Langue Francaise*, 1: 226, 1935.
16. Kaminiker, K. and Rintelen, G. Experiences with evipan in major operations. *Deutsch. Ztschr. f. Chir.*, 244: 571, 1935; through *Klin. Wchnschr.*, 14: 1515, 1935.
17. Beck, William C. The present status of anesthesia with sodium evipan. *Anesth. and Analg.*, 13: 215, 1934.
18. Baetzner, Wilhelm. A new intravenous narcosis with evipan-sodium. *Deutsch. med. Wchnschr.*, 59: 48, 1933.
19. Burkle, de la Camp, H. Evipan-sodium narcosis. *Deutsch. Ztschr. f. Chir.*, 240, 1933; through *Münch. med. Wchnschr.*, 80: 1487, 1933.
20. Ernst, Max. Evipan sodium, a new agent for intravenous anesthesia. *Münch. med. Wchnschr.*, 80: 128, 1933.
21. Gorodner, J. Intravenous anesthesia with sodium evipan. *Semana med.*, 408, 1933; through *Brit. Med. Jour.*, 1: E7 (1934).
22. Morl, F. Fatality following evipan narcosis. *Zentralbl. f. Chir.*, 1933, 15; through *Deutsch. med. Wchnschr.*, 59: 786, 1933.
23. Harms, Klaus. Dosage of sodium evipan to obtain light and short narcosis. *Deutsch. Ztschr. f. Chir.*, 241, 1933; through *Münch. med. Wchnschr.*, 81: 5, 1934.
24. Westerborn, A. Evipan anesthesia. *Nord. Med. Tidsskrift*, 997, 1934; through *Brit. Med. Jour.*, II, E-83, 1934.
25. Merritt, Edward L. The value of evipal anesthesia in urology. *Urol. and Cutan. Rev.*, 39: 709, 1935.
26. Boden. Asthma and evipan. *Münch. med. Wchnscbr.*, 81: 407, 1934.
27. Suraci, Charles. Evipal soluble—a unique anesthetic for intravenous use. *Med. Ann. District of Columbia*, 4: 29, 1935.

EVIPAL ANESTHESIA: ITS USE IN PROCTOLOGY*

BENJAMIN HASKELL, M.D. AND JOHN J. CHELEDEN, M.D.

Assistant in Proctology — Clinical Assistant in Proctology
Jefferson Medical College Hospital

PHILADELPHIA

THE extensive clinical use of evipal, as reported by numerous observers, has established the value of this newer agent in the field of anesthetics. Because it has the property of producing a short but sufficiently deep anesthesia, evipal would seem to be especially useful in proctology, where there are many procedures requiring only a brief anesthesia but relaxation must be complete. In order to determine the applicability of this agent to rectal surgery, it was administered to 100 cases, and a summary of our experience is presented in this report.

This anesthetic is characterized chiefly by its ease in administration and rapidity of induction; by its short duration and prompt detoxication; by its wide margin of safety and its rare after effects. A detailed review of the pharmacology of evipal will not be given here except to emphasize the fact that although related to amytal, nembutal and pernocton it has less than half the toxicity of these other barbiturates when given in anesthetic doses. Experimental evidence by Kennedy and Narayana and others has indicated that the drug is decomposed and detoxicated by the liver. It is not cumulative in action and animals could not be made to show any degree of tolerance after repeated injections.

A detailed clinical study was made of the effects of the administration of evipal anesthesia in the present series of cases. The pulse and blood pressure were recorded immediately before and after the administration and at five minute intervals thereafter for six or more consecutive readings. The effects on respiration were noted. The temperature was recorded before administration and upon complete recovery. The eye and other important reflexes were observed. A study of the period of reaction and the postanesthetic effects, including subjective symptoms, was also made. The effects of the preanesthetic administration of opiates in a group of the cases were also observed.

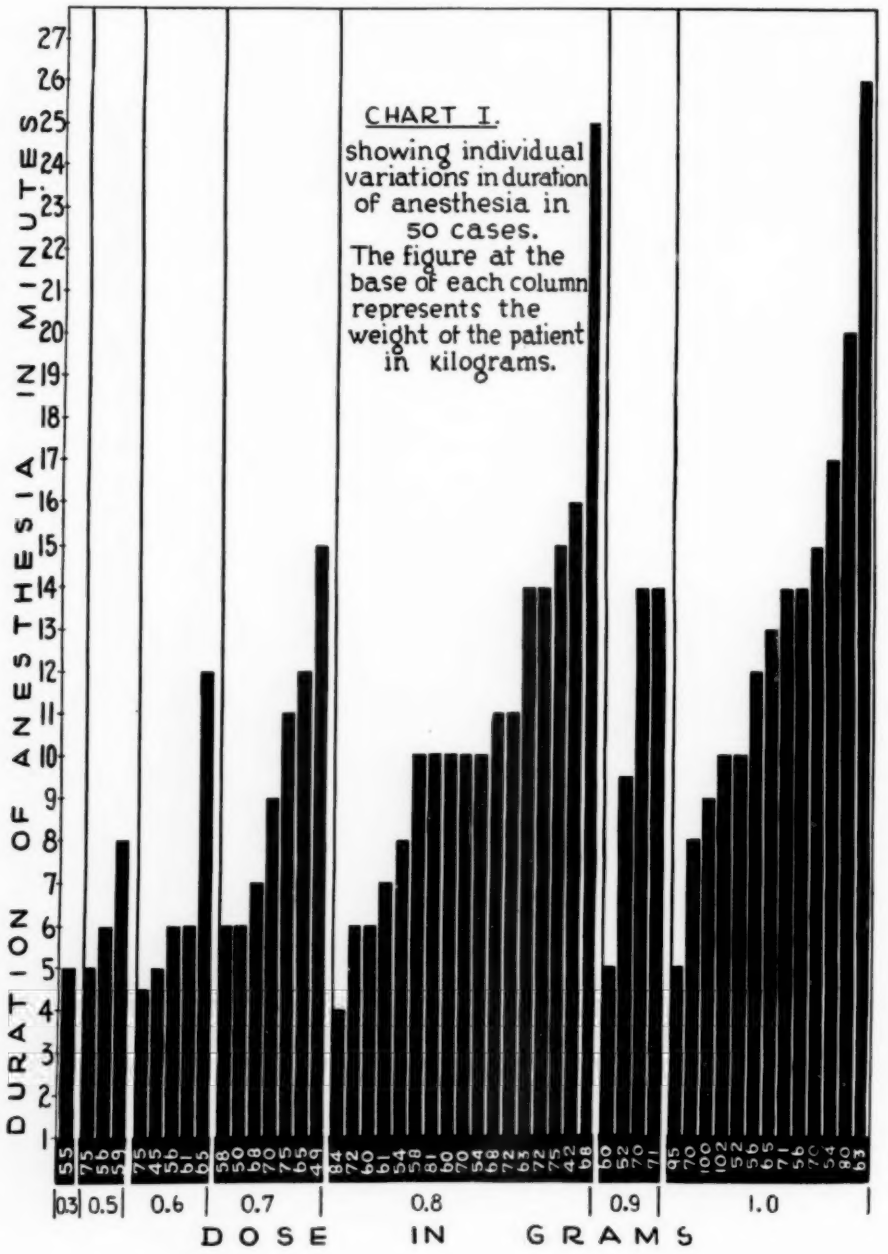
TECHNIQUE OF ADMINISTRATION

The precautions that are usually observed in administering any general anesthetic are applicable to evipal, both before its administration and during its full course of action. To secure optimum results and to avoid the dangerous effects of overdosage careful technique in administration is necessary. This is especially true in rectal surgery where a profound depth of anesthesia is essential for complete relaxation of the anal sphincters. It was found that the technique usually advised in administering evipal in other fields of minor surgery was not satisfactory in the present group of cases. In earlier reports the dose of the drug was determined according to the weight of the patient and it was then administered at one time as a single injection. However, the weight proved to be of little value as a gauge in calculating the total dose to be administered to a patient. This will be discussed later in more detail. In addition, it was found that a definite ratio between the amount of anesthetic administered and the duration of anesthesia was not the rule (Chart 1). For these reasons the following slight modification in administration was made and found to be more effective. Instead of estimating the dose beforehand, we now individualize each

* From the Department of Proctology, Surgical service of Dr. Thomas A. Shallow, Jefferson Medical College Hospital.

patient and attempt to control the anesthetic by administering it in interrupted and divided doses of 1 to 3 c.c. during the course of the operation.

fashion. The operative area is prepared and all is made ready to proceed with the operation. The second hand of a watch should be available. After the needle is



The anesthetic is freshly prepared by dissolving one gram of the drug in 10 c.c. of sterile distilled water. The injection may be made into any vein, preferably into one in the antecubital space. The arm is fastened to an arm-length board and the site of injection prepared in the usual

inserted into the vein the patient is instructed to count slowly. Injecting at the rate of 1 c.c. per ten seconds the injection is interrupted as soon as the patient ceases counting, as unconsciousness occurs. The amount required to reach this stage will vary from 2 to 5 c.c. A thirty second pause

is then allowed for complete circulation of the blood in order that the full effect of this initial dose may be observed. An amount of solution equal to the quantity necessary to induce unconsciousness is then injected twice as rapidly. The operation is now begun, the needle being left in place. If resistance or undue motion is encountered, an additional amount of 1 to 3 c.c. is given until complete relaxation is obtained. As the operation proceeds evidence of resistance on the part of the patient is used as a guide that additional anesthesia is required. It is believed that this method of administration is more rational and avoids the dangers of overdosage which may occur with a single large injection. Recently, Lundy has also advised that the drug should be given in divided doses, "much as when ether is administered by the drop method."

In the majority of cases the total quantity necessary for a satisfactory anesthesia has been 1.0 gm. or less. In 8 cases where the operation was prolonged additional anesthesia was supplied by means of nitrous oxide or ether. However, in 6 of the later cases of this series, additional amounts of evipal in excess of 1.0 gm. were administered in small interrupted doses, as described. The procedure was found to be safe and satisfactory.

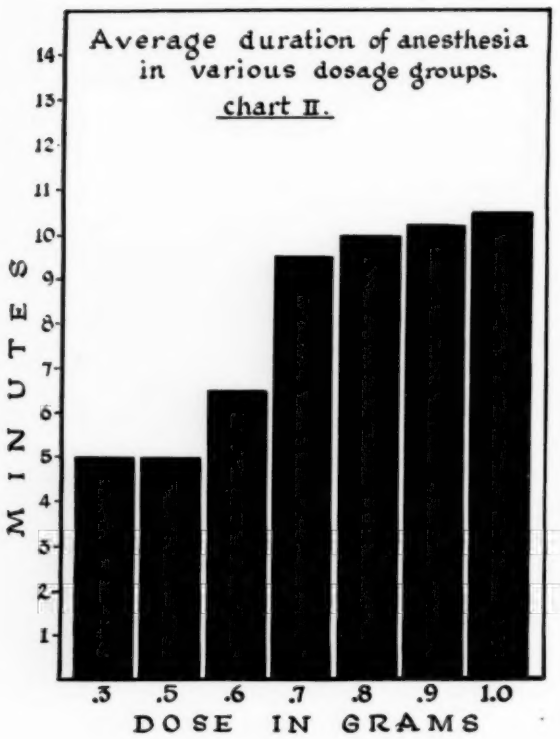
The preanesthetic administration of opiates has been advocated by many with the intention of lengthening and stabilizing the effects of evipal anesthesia. However, because of their tendency to depress the respiratory center it has been found that their use increases to a great degree the dangers inherent in the administration of intravenous evipal. Morphine, 0.016 gm. (¼ gr.) was given to approximately one-fifth of this series of cases. It prolonged and apparently deepened the anesthesia but it also lengthened the postanesthetic period of recovery and at times caused alarming symptoms during the induction period due to respiratory embarrassment. Moreover, it was noted that the ability to control and regulate the action and depth of this anesthesia, as described, was greatly decreased in those cases receiving premedication. Because of these reasons and since the induction period of evipal anesthesia is devoid of those unpleasant features usually seen in other types of general anesthesia, the preanesthetic use of opiates was regarded as unnecessary and was limited solely to the extremely nervous patient. It should be administered at least one hour prior to the time of operation and should be regarded primarily as a sedative. Premedication with other barbiturates is contraindicated because of the additional depressant action. Although it was not encountered in the present group of cases, idiosyncrasy to barbiturates occasionally exists, and it is desirable to question the patient in this respect before administering evipal.

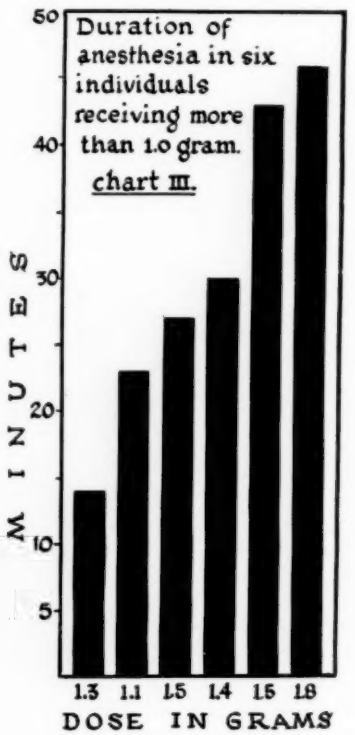
CLINICAL SIGNS AND SYMPTOMS

During the injection of the first 2 c.c. the patient counts aloud and with confidence; with 3 to 4 c.c. he hesitates as a feeling of fatigue comes over him; he becomes surprised; a vacant stare follows as intense drowsiness overwhelms him; the counting becomes disordered and whispered and finally with a deep sigh or yawn he drifts into anesthesia.

Dependent upon the amount given he partially awakes in five to twenty minutes, wearily opening his eyes, looks about for a moment and usually falls asleep again. The patient has passed through a short period of complete amnesia. Most patients will then sleep soundly for one to two hours. They should be allowed to rest for this period of time or longer. Drowsiness is usually present for several hours following the rest period. In four to eight hours the patient states that he feels well and refreshed, as if after a very restful sleep. Approximately one-half the out-patient cases were permitted to leave, accompanied by someone, after resting two hours. The remainder were retained in the hospital for a longer period.

Objectively, the respirations become slower and deeper during the period of induction. As deep anesthesia sets in they become more shallow and rapid. It is a good plan to place a wisp of cotton before the nostrils to better observe respiratory ventilation. The color remained good throughout, except in 6 instances where cyanosis was encountered. The pulse rate was found to increase ten to thirty beats per minute, the pulse volume slightly decreasing. The blood pressure falls from ten to thirty mm. of mercury. It is lowest at completion of injection and then gradually rises to normal as the patient reacts. The temperature was not affected. The pupils are mid-wide to widely dilated and always react to light. The lid and corneal reflexes are absent only during the short period of deepest anesthesia. Definite conclusions regarding the depth of the anesthesia cannot be made from observing the reflexes. The presence or return of muscular resistance was found to be a better guide to the depth of anesthesia and was thus utilized to indicate the amount of anesthetic required. The relaxation of the peripheral musculature including the abdominal walls is complete as that obtained with ether anesthesia. The anal sphincters relax remarkably well with evipal.





SUMMARY OF CASES

Evipal was administered in 100 instances to a group of patients in whom various proctologic procedures were performed. These included examinations, painful dressings and operations. The group was composed of 87 patients; the youngest was 24 years of age and the oldest seventy-one years. The doses ranged from 0.3 gm. to 1.8 gm. The anesthetic was administered twice to 6 patients; three times to 2 patients and four times to another. In those cases receiving 1.0 gm. or less the duration of anesthesia varied from four to twenty-six minutes. Only 6 patients were given more than 1.0 gm. and in these the period of anesthesia was prolonged, varying from fourteen to forty-six minutes (Chart III).

In 85 of the 100 cases anesthesia could be classed as completely satisfactory; in 8 cases as partially satisfactory and in 7 as

failures. In the partially satisfactory group the duration of anesthesia was extremely short and supplemental anesthesia with nitrous oxide gas was used. In the group classed as failures, 3 were due to underdosage and one to the fact that we failed to enter the vein fully, injecting most of the solution into the perivascular tissues. This patient later developed venous thrombosis with sloughing of the surrounding tissues. No explanation can be given for the failure in the remaining 3 cases of this group. Two of the patients coughed so violently that any operative procedure was made difficult. In the third patient, a robust individual, the agent was effective in producing only a state of hypnosis, although a total of 1.0 gm. was administered.

Undesirable effects were encountered in a small percentage of cases and were found to be most frequent where premedication had been used. Moderate resistance was encountered in 6 instances and to some extent interfered with the operation. Slight muscular twitchings were noted in 10 cases but were not troublesome. These could be traced either to underdosage, injecting too slowly or starting the operation too soon. Cyanosis occurred in 6 instances. Bringing the jaw forward and thus establishing a better airway relieved the difficulty immediately in 4 cases. In 2 of the patients who were seized with attacks of coughing the cyanosis was relieved only after the administration of oxygen and carbon dioxide. Marked postanesthetic restlessness was observed on 4 occasions. Nausea, vomiting and headache did not occur in any instance. Signs of collapse, even slight, were never encountered. In the event that respiratory spasm or paralysis does occur one should resort to the immediate administration of oxygen, together with artificial respiration, if necessary. In addition, stimulants should be available for immediate intravenous injection.

CONTRAINDICATIONS

The chief contraindications appear to be the presence of hepatic disease and any condition which produces massive interference with gaseous interchange in the lungs. So too, are conditions such as sepsis, which may cause morbid changes in the liver. One of the present cases was a patient, with extensive carcinoma of the liver, who received 0.6 gm. He did not react from the anesthesia for about two hours, although at no time did he present any alarming symptoms. The present series included 2 patients with active pulmonary tuberculosis, 2 with marked cachexia and one with recurrent attacks of auricular fibrillation. None of these showed any clinical evidence of ill effects after administration of the anesthestic. These few cases suggest the adaptability of evipal in some instances where the use of other types of anesthesia may be contraindicated.

Thirty-two fatalities have been reported following several hundred thousand administrations of evipal. It should be pointed out that many of the deaths occurred while evipal was still in the experimental stage, that contraindications had not been observed, and that many of the cases were acknowledged to be very poor risks for any type of anesthesia.

COMMENTS

As previously mentioned, earlier observers attempted to calculate the dose of evipal according to the body weight and administered the estimated amount as a single injection. After this procedure was followed in a number of the cases presented here, it was found that with a given dose no definite ratio existed between the weight of the patient and the duration of the expected anesthesia (Chart 1). It appears therefore that the weight need not be considered in the administration of the anesthetic.

Regarding the relationship of dosage to duration of anesthesia it was found that no definite ratio existed between them. It is virtually impossible in any procedure of known duration to predict the total dose that the patient will require. An extreme variability exists in the response of the

individual patient to a given dose. However, in a general way, there is some degree of relationship between the dosage and the duration. In Chart 11 the patients are grouped according to the amounts received and it will be observed that the average duration of anesthesia of each group tends to increase with increasing dosage, but not in any direct proportion.

Controllability, which is an essential feature of any anesthetic, can be obtained to some degree with evipal. Its quality of being rapidly detoxified in the body is an advantageous factor toward securing this control. Untoward symptoms suggesting that an excessive dose has been given are of very short duration because of the rapid detoxication. It is believed that the element of uncontrollability is further reduced by the careful administration of this anesthetic in small, interrupted and divided doses, as described. The rapid injection of large amounts should be avoided.

The results in the present series of cases have differed in one important feature from those reported by others and this has been in the duration of anesthesia. Instead of the fifteen to twenty minute period of anesthesia expected with the administration of 1.0 gm. it was found, in many instances, that the period of available anesthesia was not more than ten minutes for the actual operative procedure. This is thought to be due to the fact that in surgery involving the anal sphincters a greater depth of anesthesia is required than may be necessary in other areas and that the period of deeper anesthesia obtained with evipal is short in comparison to the total duration of lighter anesthesia suitable for other purposes.

An important disadvantage in the use of this agent is the occasional occurrence of such reflexes as twitching, jerking or coughing, which may prove troublesome. In addition, the unexplained failure of anesthesia in 3 per cent of the present series of cases makes evipal somewhat uncertain in its effects and therefore not always reliable.

Nevertheless, evipal has definite and desirable features. The technique of administration is simple; the induction period is short and pleasant and usually psychic shock is absent. Anesthesia is usually sufficiently deep. Its action is safe if contraindications are observed; the postanesthetic sleep is short and it can be repeated without fear of habituation. We believe that this pharmaceutical has a definite place, within certain limits, in the current field of anesthetics and that it can often replace many of these agents.

SUMMARY

Evipal was administered in 100 instances to a series of 87 patients in whom various proctologic procedures were done. In 85 administrations anesthesia was entirely satisfactory; in 8 partially so and in 7 it failed.

In a clinical study of its effects evipal was found to have but little influence on the vital centers.

To secure some degree of control of the anesthetic agent, the technique of administration has been slightly modified. After an initial dose sufficient to induce unconsciousness, additional amounts are administered in small, interrupted and divided doses, as

OPERATIONS AND PROCEDURES PERFORMED UNDER EVIPAL ANESTHESIA

	Number of Cases
Internal hemorrhoids	18
Fistula-in-ano	14
Anal fissure	13
Removal of seton	13
Anal cryptitis	6
Painful dressing	5
Anal polyp	4
Perirectal abscess	4
Infected anal papilla	3
External hemorrhoids	3
Dilatation of anal sphincter	3
Rectal stricture	3
Pilonidal sinus	2
Anal cyst	2
Painful examination	2
Anal stricture	1
Rectal polyp	1
Fulguration of inoperable carinoma of rectum	1
Biopsy of rectal tumor	1
Biopsy of inguinal node	1
	100

the operation proceeds. The weight is of little value in determining total dosage.

By this method amounts in excess of 1.0 gm. were administered to 6 patients and found to be entirely safe.

The duration of effective anesthesia for proctologic procedures was found to be considerably shorter in comparison to that available for other types of surgery.

REFERENCES

Arnett, J. H. *J. A. M. A.*, 20: 1543 (May 20) 1933.

Barlow, O. W. *Jour. Pharmacol. and Exper. Therap.*, 55: 1 (Sept.) 1935.

Buck, J. S., Hjort, A. M. and DeBeer, E. J. *Jour. Pharmacol. and Exper. Therap.*, 54: 188 (June) 1935.

Coryllos, P. N. and Bass, S. *Anesth. and Analg.*, 15: 63 (March-April) 1936.

Dallemagne, M. J. *Anesth. and Analg.*, 15: 82 (March-April) 1936.

Dille, J. M., Linegar, C. R. and Koppanyi, T. *Jour. Pharmacol. and Exper. Therap.*, 55: 46 (Sept.) 1935.

Featherstone, H. W. *Brit. Med. Jour.*, 1: 322 (Feb. 24) 1934.

Fitch, R. H. and Tatum, A. L. *Jour. Pharmacol. and Exper. Therap.*, 44: 325 (March) 1932.

Flagg, P. J. The Art of Anesthesia, Philadelphia, J. B. Lippincott Company, 1932.

Goldhahn, R. *München Med. Wchnschr.*, 80: 1640, 1933.

Gower, W. E. and Van De Erve, J. *Jour. Pharmacol. and Exper. Therap.*, 48: 141 (June) 1933.

Heard, K. M. *Can. Med. Jour.*, 31: 617 (Dec.) 1934.

Holman, A. and Mathieu, K. *Am. Jour. Obst. and Gynec.*, 30: 118 (July) 1935.

Jarman, R. and Abel, A. L. *Lancet*, 226: 510 (March 10) 1934.

Joannides, C. K. *Edinburgh Med. Jour.*, 41: 615 (Nov.) 1934.

Johnstone, I. L. *Brit. Med. Jour.*, 1: 761 (April 13) 1935.

Kennedy, W. P. *Jour. Pharmacol. and Exper. Therap.*, 50: 347 (April) 1934.

Kennedy, W. P. and Narayana, B. *Quart. Jour. Exper. Physiol.*, 24: 69 (Feb.) 1934.

Killian, H. *Anesth. and Analg.*, 13: 127 (Sept.-Oct.) 1934; 13: 227 (Nov.-Dec.) 1934.

Landau, E. and Wooley, E. J. S. *Brit. Med. Jour.*, 1: 192 (Feb. 3) 1934.

Landor, J. V. and Salleh, M. *Brit. Med. Jour.*, 2: 940 (Nov. 24) 1934.

Lask, M. and Crawford, J. H. *Lancet*, 2: 308 (Aug. 11) 1934.

Livingston, E. M., Emy, S. and Lieber, H. *Am. Jour. Surg.*, 26: 516 (Dec.) 1934.

Lundy, J. S. *Can. Med. Assn. Jour.*, 33: 490 (Nov.) 1935; *Anesth. and Analg.*, 9: 210 (Sept.) 1930; *Proc. Mayo Clinic Staff Meetings*, 10: 536 (Aug. 21) 1935.

Lundy, J. S. and Tovell, R. M. *Northwest Med.*, 33: 308 (Sept.) 1934.

Lyle, T. K. and Fenton, F. G. *Brit. Med. Jour.*, 2: 589 (Sept. 29) 1934.

Maloney, A. H. *Jour. Pharmacol. and Exper. Therap.*, 49: 133 (Oct.) 1933.

Maloney, A. H. and Tatum, A. C. *Jour. Pharmacol. and Exper. Therap.*, 44: 337 (March) 1932.

Maloney, A. H. and Hertz, R. *Jour. Pharmacol. and Exper. Therap.*, 54: 77 (May) 1935.

Morl, F. *Zentrabl. f. Chir.*, 60: 877, 1933.

Mossedegh, G. *Bull. de Soc. d'obstet. et gynec. de Par.*, 23: 490 (Oct.) 1934.

Phillips, H. *Med. Jour. and Record*, 132: 377 (Oct. 13) 1930.

Poe, J. G. Modern General Anesthesia, Philadelphia, F. A. Davis Publ. Company, 1932.

Pratt, T. W., Tatum, A. L., Hathaway, H. R. and Waters, R. M. *Am. Jour. Surg.*, 31: 464 (March) 1936.

Report of Council on Pharmacy and Chemistry, *J. A. M. A.*, 97: 1886 (Dec. 19) 1931; 101: 208 (July 15) 1933.

Reynolds, C. *Southb. Med. Jour.*, 12: 1233 (Dec.) 1932.

Slot, G. and Galley, A. H. *Brit. Med. Jour.*, 2: 201 (Aug. 4) 1934.

Stimpl, A. *Muncben med. Wchnschr.*, 80: 1492, 1933.

Vogeler, K. and Kotzoglu, P. *Der Chirurg.*, 7: 242 (April 15) 1935.

White, C. S. *Southb. Med. Jour.*, 96: 335 (July) 1934.

White, C. S. and Collins, J. L. *Am. Jour. Surg.*, 25: 131 (July) 1934.

Widenhorn, H. *Anesth. and Analg.*, 14: 136 (May-June) 1935.

Wolff, B. *Med. Klin.*, 29: 339, 1933.

Wright, A. D. *Lancet*, 1: 1040 (May 4) 1935.

GAS THERAPY*

ALVAN L. BARACH, M.D., F.A.C.P.

NEW YORK CITY

THE use of gas therapy as a conceptual entity in the general field of medicine and surgery warrants consideration and discussion. Although by definition it refers simply to the employment of gases in the treatment of disease, the use of the term gas therapy amounts to a proposal to regard the therapeutic administration of gases as part of a special branch of medicine sufficiently allied to anesthesia to warrant consideration under a combined heading "anesthesia and gas therapy."

We are bound to inquire what are the purpose and advantage of this attempt to widen the specialty of anesthesia to include the administration of gases in clinical illness.

Although oxygen therapy had been employed in medicine ever since Thomas Beddoes established the Pneumatic Institution in Bristol in 1800, the controlled effective clinical administration of oxygen was initiated only sixteen years ago by Stadie at the Rockefeller Institute, Meakins in England, and Barach, first at the Massachusetts General Hospital and later at the Presbyterian Hospital, New York. As a result of these investigations, the fundamental facts of clinical oxygen therapy were established; namely, (1) that the oxygen concentration of the arterial blood could be elevated to or near the normal value by inhalation of high concentrations of oxygen in patients with pulmonary or cardiac insufficiency, (2) that approximately 40 to 60 per cent oxygen in the atmosphere was necessary for effective employment of this therapy, (3) that efficient, comfortable and hygienic methods of administration were essential in order to obtain the therapeutic results aspired, (4) that significant clinical improvement was demonstrable when these criteria were fulfilled.

During the ensuing sixteen years the value of oxygen therapy was confirmed and clarified by the work of numerous investigators. The point chiefly to be emphasized is that wherever an understanding of the pathological physiology of oxygen-want and technical skill in the administration of oxygen have been present, the conclusion has been made that oxygen therapy, where it is indicated, has both a beneficial and, at times, a life-saving effect. At first, it was employed chiefly in lobar pneumonia, bronchopneumonia and post-operative pneumonia; later, its use was extended to congestive heart failure, coronary thrombosis, pulmonary emphysema and fibrosis, bronchiectasis, atelectasis of the lungs of the newborn. Any acute development of oxygen-want, such as that due to embolism of the lungs, serious blood loss or shock, may become an indication for oxygen therapy.

In cases in which the respiratory center was depressed, as by morphine, CO poisoning, drowning or electric shock, the addition of 5 to 10 per cent CO_2 to oxygen was advocated by Henderson to promote more rapid reversal of arterial anoxemia. In fact, this aspect of medicine has been considered worthy of separate mention in the specialty that is being discussed under the heading "Resuscitation," by the Society for the Prevention of Asphyxial Death, whose president, Dr. P. J. Flagg, has steadily advocated the formation of an alliance between anesthesia, oxygen therapy and resuscitation. In the author's view, there is no physiologic justification for the administration of carbon dioxide except in patients in whom obvious depression of the respiratory center exists. This largely excludes its use in pneumonia and in cardiac insufficiency. However, in cases where resuscitation is indicated, the addition of CO_2 to oxygen for short periods appears to be of decided value. Other procedures, such as mechanically opening the passageway to the lung, artificial respiration, intelligent use of a safe pulmotor,

* From the Department of Medicine, College of Physicians and Surgeons, Columbia University, and the Presbyterian Hospital, New York.

and the employment of drugs which stimulate the respiratory center such as alpha-lobelin, are all measures designed to provide the body with an adequate supply of oxygen to alleviate arterial or tissue anoxemia. Whether or not resuscitation appears as a separate heading in the newly conceived Section of Anesthesia and Gas Therapy is incidental. Of greater importance is the fact that a great many avoidable deaths occur from asphyxia from various causes, and that our present inquiry centers on the question whether the formation of a specialty which would develop and demand skilled training in overcoming all types of dangerous anoxemia would be of advantage to the community as a whole.

To complete the groundwork of our discussion, we have to consider the use of helium. Because of the recent intrusion of this gas in inhalational therapy, the term "gas therapy" has been selected instead of "oxygen therapy." The author has found helium to be of decided value in the treatment of intractable, severe asthma, in patients who have become refractory to adrenalin. As a result of periodic inhalations of this gas mixed with oxygen in suitable proportions, patients have recovered who appeared to be in serious, even grave, status asthmaticus. In more or less continuous asthma, with partial refractoriness to adrenalin, helium therapy has accomplished a greater restoration of adrenalin sensitivity than any other measure tried, with accompanying clinical improvement.

We have employed the helium-oxygen mixture in cases in which obstruction in the pulmonary airway produced obstructive dyspnea. The inhalation of this light gas mixture proceeds with one-half the force required to ventilate the lungs with either oxygen or air, and in some instances has been able to avert tracheotomy. In other patients, mostly children, in whom the obstructive lesion was below the site for tracheotomy, the inhalation of helium-oxygen mixtures has brought relief when oxygen alone did not alter the superficial dyspnea, although lessening the anoxemia of the patient. The basis for the use of helium is its exceptional lightness, for it is only one-eighth as heavy as oxygen. A mixture of 79 per cent helium and 21 per cent oxygen has one-third the weight of air and, therefore, according to the physical formula of diffusion of gases (the velocity of movement of a gas being inversely proportional to its molecular weight), there is twice the velocity of movement or one-half the pressure in using this gas mixture, instead of air or oxygen nitrogen atmospheres.

In pulmonary emphysema in which varying degrees of bronchiolar obstruction is generally present, the addition of this gas to oxygen accomplishes a greater relief of dyspnea than oxygen-enriched air. In the May meeting of the American Medical Association, discussion of the author's paper revealed its use during anesthesia when dyspnea due to obstruction or laryngeal spasm was relieved by admitting helium with oxygen in suitable proportions.

The review of these uses of oxygen and helium and carbon dioxide can only arouse the view that special teaching is necessary in order to understand the pathological physiology of the various conditions for which these gases are intended as well as skilled training in their administration. In the author's opinion the curriculum of medical schools, has been outstandingly deficient in this respect. Postgraduate instruction appears, therefore, to be necessary.

To consider for a moment the administration of oxygen therapy alone, there is a widespread employment of oxygen in hospitals and in private practice in which no testing of the oxygen concentration and even no conception of the oxygen concentration desired is considered. Except in a few clinics, there is no medical head to the department of oxygen therapy. Internes or nurses generally use the equipment without inspection of its efficiency or performance. In certain communities, oxygen therapy services have been established which supply equipment at emergency demand. Some of them test the oxygen concentration, others simply assure the physician that the desired amount of oxygen can be measured

by the litre flow of oxygen from the tank, a totally inaccurate statement. Not infrequently, the dosage of oxygen is decided by technicians who have no medical training, but who have had more contact with oxygen administration than the physician himself.

The administration of helium involves greater difficulties and hazards. The necessity for careful regulation of the oxygen concentration and helium supply is essential. An understanding of the physiological conditions for which it is intended is obviously requisite. Wherever a gas is to be given to a patient, whether it be oxygen, carbon dioxide or helium, there seems to be no escape from the conclusion that medical responsibility for its administration should be vested in a physician appointed for this purpose. The factors involved are so frequently interwoven with the life or death of the patient that relegation of gas therapy to the superintendent's office, the internes or nurses appears a dangerous and unjustified procedure.

It seems to the author that any physician who is interested in the physiology of respiration might properly assume this function, whether he be an internist or an anesthetist. There has been evidence of increasing interest on the part of physicians specializing in anesthesia to control this relatively new field. The author has undertaken a postgraduate course in this subject in which a certain society of anesthetists has expressed its desire to take part. From their previous training in the administration of anesthetic gases, the physician anesthetist feels that he has a foothold, as it were, on the general subject. However, more technical training is necessary. Furthermore, unless a purely technical oversight is accomplished, additional instruction in the pathological physiology of respiratory and cardiac illness becomes a necessity. No difficulty may be experienced in suggesting and maintaining an atmosphere of 50 per cent oxygen in a patient with pneumonia. However, the treatment of the patient with emphysema or pulmonary fibrosis raises many problems such as that of initial oxygen treatment, gradual modification of the dosage used, the type of permanent oxygen therapy the patient is to have, and also the handling of a patient with a progressive process which steadily impairs pulmonary function.

A movement such as has been proposed, namely, to qualify physicians in anesthesia and gas therapy, has a better chance of equipping hospitals and communities with experts in this field than a more random policy of allowing the subject to take care of itself. At the same time, no physician interested in pulmonary disease or internal medicine is excluded from a more special application to the physiology and treatment of disturbances in the function of the lungs and the pulmonary airways. The author knows of no way at the moment by which this special instruction may be obtained except through postgraduate teaching, most conveniently in the form of course from accredited clinics which especially emphasize the subject matter which has been discussed.

SUMMARY

The function of the gases used in medicine, oxygen, helium and carbon dioxide, has been discussed in respect to (1) the conditions for which they are intended, and (2) the technical aspect of administration.

The need for special training and medical responsibility wherever gas therapy is used has been stressed. The formation of a specialty or section tentatively called "anesthesia and gas therapy," which would qualify physicians to include gas therapy as well as anesthesia, might provide a source of intelligent and expert supervision of administration of the gases used in medicine and surgery. At the same time, no physician in internal medicine would be excluded from a special application to this field. The present widespread lack of definite medical responsibility in the administration of oxygen would be even more serious if it were extended to helium therapy. The physician who is equipped by proper training to take over gas therapy, as it has been explained in this paper, would appear to be of real service both to the medical and lay communities which at present may be unequipped in this respect.

RESUSCITATION

P. J. FLAGG, M.D.

NEW YORK

RELATIONSHIP OF ANESTHESIA AND ASPHYXIA

WHETHER unconsciousness is deliberately induced by an anesthetic agent, or accidental, as in the case of carbon monoxide poisoning, submersion, asphyxia neonatorum, etc., the anatomical and physiological result as it becomes apparent in the musculature, the reflexes, respiratory and circulatory phenomena, may for all practical purposes be regarded as identical.

The overlapping of these two fields, anesthesia and asphyxia, occasionally occurs as the result of simple anoxemia during the early induction of an anesthetic. It is a well known fact that deliberate limitation of oxygen at this time hastens the loss of orientation and voluntary coordination.

Fatal accidents also occasionally occur during the induction of anesthesia as the direct result of respiratory obstruction or by reason of an accidental anoxemia from pure nitrous oxide, pure carbon dioxide, or some other agent. In asphyxia, the early stages of unconsciousness, accidentally induced, reveal active, deep reflexes, muscle spasm and a respiration and a circulation quite intact. In accordance with the etiological cause of the accidental unconsciousness, the rapidity with which muscle tone is lost, reflexes disappear, and the respiration and circulation become embarrassed, vary widely, i.e.: unconsciousness from foreign body obstruction with a completed cycle of excitement, rigidity and relaxation may be expected to occur within five to ten minutes. Unconsciousness from carbon monoxide, from terminal poliomyelitis or from drug poisoning, may require hours to complete the fatal cycle. Regardless of the cause, however, the treatment to be applied at any given stage of unconsciousness is the same.

The physician, therefore, who is trained in the care of the patient whose unconsciousness he has artificially induced, is de facto prepared to care for unconsciousness due to accidents.

The importance of this fundamental principle cannot be over-emphasized and until it becomes generally recognized and accepted the anesthetist will not be called for the care of emergencies which by reason of his training, he is qualified to treat.

The terminology employed to designate the physician who specializes in the production of artificial unconsciousness, namely, the anesthetist, by focusing attention upon the control of pain, is unduly restrictive.

It has been pointed out on many occasions that the induction of such artificial unconsciousness is produced, in by far the larger percentage of instances, by the administration of gases and that by reason of this fact the anesthetist can be regarded as one who specializes in the use of gases, or as a gas therapist. The term, gas therapy, however, while simple and descriptive leaves much to be desired. A more scientific designation, including the science of the use of gases, is suggested in the term, pneumatology. ("pneumon," lung, "pneumatics," air, "ology," science). Pneumatology, pneumatologist, pneumatotherapy are all easily remembered.

It is an open question whether it be desirable to replace a terminology, so well installed in the minds of the profession and the laity as "anesthesia" by a new terminology however logical and satisfying. The need will eventually decide the choice. Accepting matters as they now stand, we can but do our best to explain repeatedly and upon every possible occasion, that the

duty of the anesthetist is not limited to inducing unconsciousness. He is obligated as well to equip himself to return the patient to consciousness. Recovery can no longer be left entirely to the patient's vital processes. Knowledge and equipment must be constantly available to supplement normal reactions. When the public has been impressed by the fact that the anesthetist is quite as capable of recovering consciousness as he is of destroying it, he may then expect to be called when an unconscious patient suddenly demands treatment.

CAUSES OF ACCIDENTAL ASPHYXIATION

Conditions which not infrequently cause accidental unconsciousness and death by acute or subacute asphyxiation are familiar to every physician and may be noted as follows:

Asphyxia neonatorum occurring by pressure, maternal medication, foreign body obstruction, atelectasis, and in prematurity;

Carbon monoxide poisoning occurring through the progressive elimination of the hemoglobin by the substitution of carbon monoxide hemoglobin closely resembles the effects produced by progressive hemorrhage;

Submersion in which unconsciousness occurs as a direct result of spasm, shock and foreign body obstruction;

Allergy, either obstruction by a sudden glottic edema or as a cardiac depressant;

Strangulation, a type of pure obstruction;

Chemical poisoning in which irritant vapors are inhaled, producing a pulmonary or a glottic edema with a resultant anoxemia;

Acute alcoholism, which acts as a respiratory depressant, a relaxant of the soft tissues of the airway, creating an unrecognized foreign body obstruction with or without cerebral edema;

Electric shock, in which the circulation is directly affected, and in which a fatal result follows ventricular fibrillation;

Terminal poliomyelitis, where the respiratory act in as far as it depends upon the respiratory muscles gradually fails from motor paralysis;

Drug poisoning, in which the respiratory center progressively loses its irritability, and in which the increasing anoxemia from respiratory obstruction complete a vicious cycle;

Infections of the airway, which create a progressive respiratory obstruction, or the phenomena of drowning when an abscess discharges into the trachea;

Tumors, either within or without the respiratory airway whose presence becomes fatally apparent by sudden strain or change in position;

Atelectasis of the newborn, where the ordinary pulmonary area available for respiration has failed to come into play, or where bronchial obstruction has caused collapse of the lung;

Acute pulmonary involvements of an infectious nature, where the pulmonary absorbing area is reduced by edema, obstruction or circulatory failure.

A Large Personnel Required. Without exception each of the foregoing forms of asphyxiation yield to treatment embodying the same fundamental principles.

It also becomes clear from the foregoing considerations that a substantial and well trained personnel must be developed and coordinated to care for this increasing field of service. This is true, not only in the technical assistance offered by the first-aid groups, but by the medical personnel, as well. The physician is responsible for the training of the technician as well as for the supplemental scientific work which must follow first-aid relief.

The first-aid groups necessarily constitute a much larger personnel than does the medical. It is even now very well organized and trained to carry out recognized procedures. The outstanding weakness in the system as it now functions is the lack of coordination between the technician and the physician, specifically trained for the care of the unconscious patient, namely the anesthetist. As one goes over the list of instructors and demonstrators to first-aid

squads, it is the exception to find an anesthetist in charge. The instructor is more frequently an internist, a laboratory man, or anyone else who is sufficiently "community minded" to take the responsibility for such instruction. These statements are by no means intended as a disparagement of the excellent work which has been accomplished. It is in the nature of a reproach to the anesthetists who should be actively engaged in this work. Included within the technical groups, which practices gas therapy, is to be found the first-aid squads of the Fire Department, the Police Department, the utilities, and the industries, as well as the nation wide group of volunteer life-savers, who are about to organize and to incorporate their 200,000 members. Among these are also to be noted thousands of adults and children who have been taught first-aid resuscitation measures for use in emergencies. The technical group, standing closest to the medical profession, the members of which are frequently highly trained not only in problems of first-aid resuscitation, but in the technique of medical procedures as well are the nurses who administer anesthetics.

Unfortunately, other nurses untrained in the technical administration of anesthetics are, as a rule, quite ignorant of even the more simple first-aid measures of resuscitation. They are, of course, familiar with the theory of such procedure, but their practical usefulness in an emergency is demonstrated rarely.

Among graduate physicians, and in the dental group with the exception of those who have to do with the administration of anesthetics, little stress is laid upon accidental unconsciousness. The halo of medical authority appears to be capable of supplying this deficiency. The individual physician may be faced with an acute asphyxial emergency once every two or three years. It is quite likely that, unless forwarned, he will not recognize it as such, if it falls into one of the less usual forms already mentioned. As a consequence, he does not regard asphyxia of sufficient importance to prepare himself to meet it. He fails to realize that deaths from such causes, aggregate more than 50,000 a year, or twice as many deaths as those due to automobile accidents. Many of these deaths could be averted, by familiarity with the comparatively simple technique of resuscitation.

When current medical practice becomes a chapter of historical medicine, our descendents will probably find nothing more absurd in our methods than the practice not infrequently indulged in by the physician and the surgeon, of calling a fireman or a policeman or some other lay person to take charge of his desperately ill, asphyxiated patient. This absurdity reaches a climax when such lay groups are called into the operating room.

It is conceded that the morale of the anesthetist has been almost extinguished by reason of the practice which has permitted the administration of anesthetics to be done by technicians. In many instances the medical man administering anesthetics is regarded as little more than a glorified technician, capable incidentally of carrying part of the medical responsibility, should an accident occur, and the hospital or the surgeon be sued for negligence. A strong movement is under way to "resuscitate" this morale. Unfortunately, it is faced by the apathy and the technical ignorance of thousands of young surgeons who were brought up with the assumption that anesthesia was thoroughly cared for in every respect by the nurse-technician, employed by the teams with which they worked.

ADVANTAGES OF A NEW TERMINOLOGY

This liability assumed during these years by the terminology, "anesthesia," is one of the important reasons why a new terminology, inclusive in its scope, is greatly to be desired. Such a new terminology would immediately re-orient the personnel, and limit the technical worker to his proper sphere of activity. The anesthetist would be credited with the wide field of knowledge which he has always

possessed, and in many instances he would be called, not as an assistant, but in full charge of the emergency. The "pneumatologist" would be familiar with the employment of gases for the control of pain, as is now practiced in anesthesia, for the saving of life, as it now takes place in resuscitation, and for the treatment of clinical disease by oxygen therapy using helium or any other vehicle which may be appropriate. To him would be accorded the direction and the instruction of the anesthetic technician, the first-aid squad and the large group to whom so much of the oxygen therapy technique is now being delegated. In the adoption of such terminology it may be objected that anesthesia as it has been known, as it has been practiced, and in many instances as it has been sold, will lose "face." It is felt that when the qualifications of the "pneumatologist" becomes generally understood, the assistance which he is specifically trained to render, will be recognized and his services will be sought.

Regardless of the terminology employed, the anesthetist will by the nature of his daily work hold the key to "pneumatology." Techniques developed for the care of unconsciousness artificially induced will promptly become available for accidental unconsciousness. Many procedures employed in resuscitation must be taught through the help of the anesthetized patient. It is only by this training that the occasional accident can be averted. The organized and nation wide efforts now being made by anesthetists to place anesthesia in its proper relationship to other specialities is to be supported by every means at our command. One of the outstanding figures of this movement, Dr. Paul M. Wood of New York City, has sacrificed much and has accomplished astonishing results by his persistence and spirit of cooperation.

USE OF COMPLICATED APPARATUS

From the foregoing it may be seen that the lack of general information concerning the anatomical and physiological background of asphyxia has contributed largely to the widespread distribution of mechanical robots for artificial respiration. A machine devised to operate with clock-like precision, which will deliver a set rate, rhythm and amplitude of respiration appears to meet the ideal requirements. So many physicians have become satisfied to leave the explanation and the treatment of resuscitation to lay groups and individuals that they accept the demonstrations of the highly trained pressure salesman with little or no resistance. Owing to their unfamiliarity with the fundamental issues involved, they entirely overlook the fact that every asphyxiated patient presents a specific problem, that the conditions of this problem vary rapidly, under treatment, or by merely being left alone. A theoretical rate and rhythm of respiration, suitable for one patient will serve to inhibit the slowly returning voluntary control in another patient. A theoretical volume of oxygen gas blown to a patient seldom relieves such a patient, unless such a volume can be introduced past all obstruction to the spot where it will do the most good. The flooding of the hospital market with such devices does nothing but obscure the real issue of resuscitation. It leaves the physician, the interne and the technical worker complacantly trusting that the machine is doing the work for him, and that all is well. Failures of the machine are explained away as unavoidable accidents, and resuscitation which takes place in spite of the treatment, are referred to as remarkable successes. At no time is the operator in actual contact with the physiological responses of the patient. Such a patient either corresponds with the mechanism employed, or he does not recover.

It is urged in this communication that equipment for artificial respiration be of the utmost simplicity and designed for a specific objective. It is believed that the purpose of artificial respiration is first to stimulate an absent or a depressed respiration, secondly, to follow this newly estab-

lished rate and rhythm, and to amplify it instead of attempting to lead it. For this reason, all equipment based upon the principles of the original pulmotor should be discarded. Such equipment offers no mysterious advantages. Medical literature of the last twenty-five years confirms this vew.

Negative pressure cabinets are invaluable in selected cases. Their function is to replace muscular action, but they must be employed with a full understanding of other respiratory requirements. They are not adapted to the care of sudden respiratory emergencies, but are well suited to the maintainance of artificial respiration over periods of hours, days and weeks.

INSTRUCTION OF TECHNICIANS

The technical personnel may well be taught and should be intimately familiar with the objective to be obtained and the mechanical means provided to secure the end in view. A brief and graphic description of the anatomy and physiology of the respiratory tract should precede all practical work. The mechanics of normal ventilation should be stressed, and the obstacles encountered to this normal ventilation should be pointed out. Ordinary and animated motion pictures are invaluable for this purpose. The problem of respiratory obstruction should be thoroughly understood.

These preliminary considerations will provide a reasonable basis for the explanation and the practice of the prone pressure technique in the average case and the Sylvester method in the exceptional case. The reasons for the use of oxygen in addition to mechanical manipulation and the addition of CO_2 to this mixture for the stimulation of the respiratory center can be made quite plain to the ordinary layman. The complications offered by active reflexes and muscle spasm should be emphasized.

Following a clear understanding and a practical working knowledge of the postural methods of artificial respiration with or without the use of an inhalator with its oxygen and carbon dioxide, members who have shown themselves adept should be taught the use of the nasal catheter and the insertion of the pharyngeal airway. A nasal catheter of suitable size, lubricated by the patient's saliva and passed into a nostril is much less likely to be followed by traumatic after effects than is the routine practice of attempting to separate teeth, closed in spasm, and the subsequent procedure of grasping and pulling the tongue forward. Oxygen blown through such a catheter past the base of the tongue into the open pharynx is a life-saving procedure. It will break the vicious circle of accumulating anoxemia and allow the patient to recover active reflexes and consciousness. Such an oxygen flow supplied by a light weight rubber bag will not accumulate enough pressure to do damage. Where ready introduction of a catheter into a nostril is prevented by a deviated septum or enlarged turbinates, the oral tube should be employed. Such a tube should be of exceptionally heavy gauge metal in order that it may present a velvet edge.

By the use of a nasal catheter, a patient who is breathing in even the most shallow manner will recover much more quickly than with the most vigorous postural manipulations. Furthermore, he may be immediately transported under such treatment and removed from the site of the accident without discontinuing the insufflation of oxygen.

In addition to supporting and stimulating the respiration, the circulation should receive prompt attention. The patient should be covered with warm blankets and removed from exposed surroundings. The circulation follows the respiration very closely. A depressed or absent respiration will promptly be followed by a rapid running, almost imperceptible pulse, except in the case of the occasional florid individual, when a rapid bounding pulse may be present until close to a fatal termination. On the other hand, a circulation depressed from shock by exposure will not pick up the oxygen made available by artificial

respiration, unless this should be present in a concentrated form. It is, therefore, highly important that the circulation as well as the respiration should receive adequate and prompt attention.

MEDICAL CARE

Submersion experiments on dogs conducted by Coryllos suggests a sequence of four stages in drowning: initial apnea from shock of inspired fluid, dyspnea from accumulating CO_2 stimulation, terminal apnea from respiratory center fatigue, and apparent death, in which the respiration has disappeared and the circulation is faint or imperceptible. The medical man called to attend a patient to be resuscitated is not likely to meet the patient in the first two stages of initial apnea and dyspnea. The patient will be presented to him in a state of terminal apnea or apparent death. Occasionally, those who have received adequate first-aid treatment in the early stage of terminal apnea may have recovered to such a degree when the physician arrives that he finds the reflexes have returned, the circulation and the respiration embarrassed, but not critically effected. A breathing patient will pick up oxygen and carbon dioxide offered to him by means of an inhaler by nasal or by oral tubes. Where active reflexes have returned, an inhaler is the best technique. On the other hand, should there be severe masseteric spasm, and mucus or vomitus in the airway, an inhaler will not prove as effective as a nasal tube combined with suction.

In practice, it has been the custom to divide asphyxia into three stages: (1) the depressed patient who can be roused, (2) the unconscious patient who cannot be roused, with intact circulation and respiration, with or without muscle spasm and reflexes, and (3) the unconscious relaxed patient whose reflexes have disappeared, whose respiration has failed or completely disappeared, and whose circulation is impaired. Patients in the second stage through faulty treatment and the development of a vicious circle ultimately find their way into the third stage. With proper treatment, they will pass back into the first stage and recover. The technician is instructed to send an immediate call for medical assistance whenever he is faced with an unconscious patient who cannot be roused.

The writer is convinced that the completely relaxed unconscious patient presents indications for a specific sequence of treatment. These indications are as definite and as plain as the surgical indications, evident in an operative case.

First of all, the field should be exposed and examined, by a suitable flash light laryngoscope; secondly, foreign matter should be removed from the field by some form of suction, sponges on forceps, etc., and third, the administration of the life-saving gases, oxygen and carbon dioxide, should be introduced directly into the field at a position where they will be most effective, namely within the trachea. A detailed consideration of this technique has appeared repeatedly in previous articles.* To the writer's mind, there is no substitute for this technique in the emergency treatment of profound asphyxiation. The absurdity of applying a mask and attempting to resuscitate a patient by interrupted intrapharyngeal pressure, immediately becomes apparent to one who has taken the trouble to familiarize himself with the simple technique of intratracheal insufflation. In the case of acute asphyxia occurring in the operating room, the mere act of lifting the tongue by the lip of the laryngoscope often serves to permit the patient to recover by his own voluntary efforts.

* Flagg, P. J. Intratracheal inhalation. *Arch. Otolaryngol.*, 5: 394–399 (May) 1927; Intratracheal inhalation anaesthesia, 7: 156–164 (Feb.) 1928; The exposure and illumination of the pharynx and larynx by the general practitioner, 8: 716–717 (Dec.) 1928; Asphyxia in the adult and the newborn, 12: 23–30 (July) 1930; Intratracheal inhalation anaesthesia in practice, 15: 844–859 (June) 1932; Art of Anaesthesia, Ed. 5., Phila., Lippincott Co.; P.A.D., prevent asphyxial death, *Hygeia*, 14: 32 (Jan.); 158 (Feb.); 233 (March); 335 (April) 1936.

The patient may now be removed safely from the site of the accident as soon as he has received the attention of the trained physician. The circulation of a patient who has ceased to breathe may be satisfactorily supported for hours by the intratracheal insufflation of oxygen. With an intrapharyngeal or an intratracheal tube in place, the patient may be safely transported to the emergency ward of the hospital, where upon his recovery he can be placed in bed and given adequate oxygen therapy treatment.

The writer's experience indicates that the prevention of asphyxial death, in as far as a physician is concerned, turns upon the popularization of laryngoscopy in the relaxed patient. The so-called death zone occurring between the epiglottis and the glottis should become merely a historical memory instead of an ever present threat.

CONCLUSIONS

The question of resuscitation has been considered from its philosophical angle rather than from the point of view of technique. The natural relationship of anesthesia and asphyxia has been indicated. The restrictive nature of the popular terminology has been questioned and a more inclusive term is advocated. The personnel necessary to the adequate application of resuscitation measures has been pointed out. The integration of this personnel under the direction of the anesthetist is advocated. Reference has been made to the technique available for the first-aid worker and suitable technique for the physician has been suggested. The conviction is stated that the success of resuscitation measures applied by physicians turns upon the popularization of laryngoscopy and the elimination of what has been known as the "death zone" of the respiratory tract.

OBSERVATIONS ON THE USE OF TRIBROMETHANOL (AVERTIN)

PAUL M. WOOD, M.D. AND ROBERT S. BICKLEY, M.D., F.A.C.S.

Assistant Clinical Professor of Anesthesia — Clinical Professor of Surgery

New York Medical College and Flower Hospital

NEW YORK CITY

THE observations covering a period of seven years of more than 4800 administrations of avertin* by various methods and many combinations of supporting agents are presented. As it is still a relatively new agent there is much discussion of its fields of usefulness, indications, contraindications and value. This report also reviews a technique for determining dosage, preparation and administration for basal narcosis, based on 2700 cases.

The history of avertin began in 1923 when Willstaetter and Duisburg[1] discovered the white crystalline powder resulting from the yeast fermentation of bromal. Under a different name it was used by oral administration for the relief of whooping cough in children[2] but this method proved unsatisfactory and it was tried by rectum. The prolonged sleep, somewhat like that produced by hedonal was noted. In 1926 Eichholtz[3] suggested its use for anesthesia in clinical surgery in Europe. Shipway[4] and others began the use of avertin in England in 1928 and have reported large series of cases, as have Krieselman[5] in 1931, Bourne[6] in 1934, Mueller[7] and Wood[8] 1936, and Maddox published a book in 1931.

When avertin first was used to produce narcosis the pure powder form was employed. In order to facilitate mixing and to secure a more stable form of this agent, the powder was dissolved in amylene hydrate, called avertin fluid and is now universally used in this form, 1 c.c. of the fluid representing 100 mg. of tribromethanol. At first complete anesthesia was sought and the drug was administered in dosages calculated to produce this effect. The experimental and clinical methods of administration of both the pure form and the fluid form were by vein, subcutaneous injection and rectum. The subcutaneous use of the agent appears to have been limited to laboratory experiment.[2] Endovenous use of the drug prepared from the crystals gave a very unreliable anesthesia as regards depth and duration. The dose was prepared similarly to that for rectal use, except attention to have all parts of the apparatus sterile was most rigid. The amount necessary for endovenous anesthesia is about one-third that estimated for rectal use.[9] Results with the fluid form were definitely better than with the pure preparation, but the cumbersome apparatus, the exact timing of procedures and the necessity for strict sterility caused this method of administration to be discontinued.

The chemistry and pharmacology[10,11,12] of avertin has been reported in detail. Special reports of the toxic effects on the liver,[13] heart,[14] brain,[15] kidneys[16] and pancreas[17] have been presented. It should be noted that the depression of the respiratory center observed with the use of avertin crystals is less when avertin fluid is used. Amylene hydrate solvent of the latter preparation is a central stimulant. This may account for different actions reported by early observers using the crystalline form of the drug.

Avertin was used alone for both surgical and medical purposes as in the treatment of strychnine poisoning,[18,19] angina[20] and

* "Avertin" as used in this report refers to the commercial preparation, "Ethobrome" or "Avertin Fluid," which is tribromethyl alcohol dissolved in amylene hydrate.

tetanus.[21,22] Many minor procedures could be satisfactorily performed, as the removal of warts, lipoma, small cysts and even amputation of digits, and as complete anesthesia for the surgical procedure of esophagoscopy and dilatation of congenital stricture. The following case illustrates the successful use of avertin in such a surgical procedure.

Case 1. J. L., male, aged thirty years, single, clerk, six feet height, 129 pounds on July 6, 1934. Physical examination was negative except for a slight "tobacco" cough and the surgical condition of congenital stricture of the esophagus. His history was negative. The operation proposed was esophagoscopy and dilatation of the stricture under avertin for complete anesthesia. Preanesthesia findings were a blood pressure 118/60, temperature 98.6° pulse rate 80 and respiration 20; mental attitude was alert, calm and cooperative. Preliminary medication was magendie solution m. 5, and scopolamine gr. $\frac{1}{150}$, by hypodermic injection at 11:40 A.M. At 12 noon 4.7 c.c. of avertin fluid was mixed and administered, which is an 80 mgm. per K. dose given in 2.5 per cent dilution with tap water by rectum. Sleep began at 12.08; he was moved to the carriage and taken to the operating room at 12.25. The intended operation was completed in an entirely satisfactory manner from 12:50 to 1:15 P.M.

During the following two years this patient has had repeated administrations of avertin. The second administration was similar to the first but was not sufficient for the entire procedure although the dose was regulated for the increased weight of 134 pounds. The operative work lasted nineteen minutes, but it was necessary to use intranasal nitrous oxide-oxygen the last five minutes. For the next administration the amount was increased to 85 mgm. per K. dose. The patient arrived in the operating room conscious but was easily controlled with a few inhalations of nitrous oxide-oxygen for three minutes. The operative time was fourteen minutes. On his next admission the dose was estimated at 100 mgm. per K. No preliminary hypodermic was given. Nitrous oxide-oxygen and ether had to be used throughout the entire procedure. On September 13 he received hypodermically morphine $\frac{1}{4}$ gr. with scopolamine $\frac{1}{100}$ gr. at 11:30 A.M. His weight was now 142 pounds. A 125 mgm. per K. dose of avertin was prepared as before. The increase here was due to the report of another anesthetist that two weeks previously this preparation with a 100 mgm. dose was only partly satisfactory. This time there was perfect anesthesia. It has been necessary to increase the mgm. per K. dose with each subsequent anesthetization.

The patient is in the best of health at the time this report is being prepared, (August, 1936) weighs about 180 pounds and requires nearly 180 mgm. per K. with a hypodermic of morphine sulphate gr. $\frac{1}{4}$ and atropine sulphate gr. $\frac{1}{120}$ given one and one-half hours prior to operative procedure. The avertin is administered about thirty minutes before operation, but the last two times the anesthesia had to be supplemented with nitrous oxide-oxygen-ether and once with cyclopropane oxygen.

This case illustrates the use of avertin for complete anesthesia. It also shows a development of tolerance for avertin as reported by others. In all the administrations there was no untoward finding except following the third operation. The patient was able to eat thickened soups for the first time in many months. He reported a slight colitis with definite abdominal distention and "cramps" on the third postoperative day, which disappeared within a few hours. The family physician and surgeon agreed with the anesthetist that the colitis was not referable to the rectal use of avertin. The first time he was treated was the only occasion when the patient remained in the hospital for more than one postoperative day.

Another interesting case illustrates the use of avertin in extensive dressings and also shows avertin tolerance.

Case 11. J. M., a male youth, twelve to thirteen years, emaciated, pale, alert, cooperative and recovering from osteomyelitis had multiple dressings, nine in all, and two very extensive, which required almost an hour to change twice a week. This boy began on a rectal dose of 80 mg. per K. His general condition improved slowly but steadily. His dose was kept level with the weight increase for two or three dressings and then it would be necessary to repeat the administration using one-fifth of the original amount in addition or use gas or ether as the effect did not hold through the long dressing. The doses were then

regularly increased in amount and for many months this procedure was followed until the patient was sent to a convalescent camp at which time his avertin requirement for forty-five minute dressing was almost 225 mgm per K. Occasionally he would have slight nausea and vomiting after awakening. Usually there was no "after effect." Rarely there was a mild postanesthetic headache.

These 2 cases show that avertin may be repeated many times without producing harmful effects.

In a third type of case favorable use has been made of avertin in the treatment of alcoholic delirium.

Case III. T. W., a male, thirty-two years old, lawyer, single, overworked and "keeping up" on alcohol came into the hospital for appendectomy. After an easy and successful operation under routine preliminary medication of morphine sulphate gr. 1/6 with atropine sulphate gr. 1/150 given one and one-half hours before operation, followed by a dose of avertin about 74 mgm. per K. supplemented during the operation by cyclopropane oxygen and 6 c.c. of ether, he reacted normally for about six hours. His weight was 165 pounds. He began to be more than usually nervous and irritable, then definitely began to have delirium. Avertin 80 mgm. per K. was given rectally with a subsequent sleep of five hours. On awakening from this sleep he passed a normal day but the next evening had a recurrence of his tremors and delirium. Again a similar dose of 80 mgm. per K. was used and the patient made an uneventful and complete recovery.

In the early work with this new agent the greatest care was taken to follow exactly the manufacturer's instructions as to dosage and preparation. Experience at first was not alarming and the series grew till more than 300 had been completed. Increasingly favorable reports from laboratories and individuals as to the new uses and relative safety of this agent were made, even in the doses then generally accepted. These were from 100 to 150 mgm. per kilo. Still in the operating room and the recovery rooms of hospitals, patients too often needed stimulation or resuscitation. Soon thereafter came the general use of the "basal" dose of avertin by rectal administration. In some patients the estimated basal dose proved to be a complete anesthetic dose. In very rare cases it did not suffice to produce any anesthesia or only to the excitement stage.

Avertin is destroyed in the liver and excreted by the kidneys in much larger doses than are required for basal anesthesias. In suspected cases of renal or hepatic dysfunction it is wise to avoid the use of avertin. This is emphasized in spite of the fact that numerous cases of such proved lesions have been anesthetized with avertin and have appeared to make normal recovery. This is believed to be merely a fortunate coincidence rather than a routine finding. A review of the cases in which some untoward symptoms did develop, about 20 in all, a large number showed findings of some liver pathology on taking a more careful history. The recent investigations of liver death by Boyce and others[23] may give the clue to some of the unexpected postanesthetic findings, in the use of avertin.

Avertin has a depressing action on the respiratory center but does not increase intracranial pressure, an effect of most drugs which are central depressants. With avertin a quiet patient and a relatively dry field make it a satisfactory agent in brain surgery.[15] Avertin in thyroid surgery[24] has been very satisfactory. Under avertin basal narcosis many patients can be safely and comfortably operated on who previously had arrived at the operating room in such a state of excitement with tachycardia that the operation had to be postponed. Dental[25] and tonsil[26] operations have been carried out with great comfort to both the operator and the patient in the presence of this basal anesthesia. When avertin is administered for dental or tonsil operations preliminary hypodermic injection of morphine and atropine has not been used in this series in order to facilitate rapid recovery. The possibility of aspiration of blood or mucus in these cases, and

the complaint of lack of phonation in thyroid surgery may in great part be overcome. Avertin anesthesia is less controllable than inhalation types, but with the modern knowledge of carbon dioxide-oxygen, and analeptics as coramine, metrazol, picrotoxin and intravenous infusions of glucose, it becomes almost a reversible process.[8]

Another field of usefulness is in vaginal or rectal operations. The objection that the operating field is often soiled, may be overcome by administration of a smaller quantity of slightly higher concentration of the avertin, which has been found to be non-irritating in 3 to 3.5 per cent solution, and by properly timing the instillation—at least forty-five minutes before the operation. In some instances the rectum has been flushed out after the patient is asleep, but this is not essential for the small amount of the injection is almost entirely absorbed during the half hour following instillation.

One of the most exacting fields in surgery, cataract operation, has been made easier for the surgeon and patient[27] by the use of local anesthesia in combination with avertin basal anesthesia. The lack of nausea and vomiting and the quiet easy awakening in most cases is of great benefit here. The use of avertin alone for this operation was not successful on several trials, but the addition of local anesthesia eliminated all difficulty. In both normal and operative obstetrical procedures, avertin has given varying results. Tannenbaum[9] reported 75 cases in which both endovenous and rectal administration was used but it was discontinued as relatively unsatisfactory. Endovenous administration was complicated, and rectal instillation could not be given at the most desirable time, as the technique for determining the best indication for beginning the basal anesthesia was not developed. Therefore some patients had too little relief and a few were over-narcotized. In observing his series it is important to note that the infants did not need resuscitation, a fear and fact found in some reports, probably because no other preliminary medication had been used.

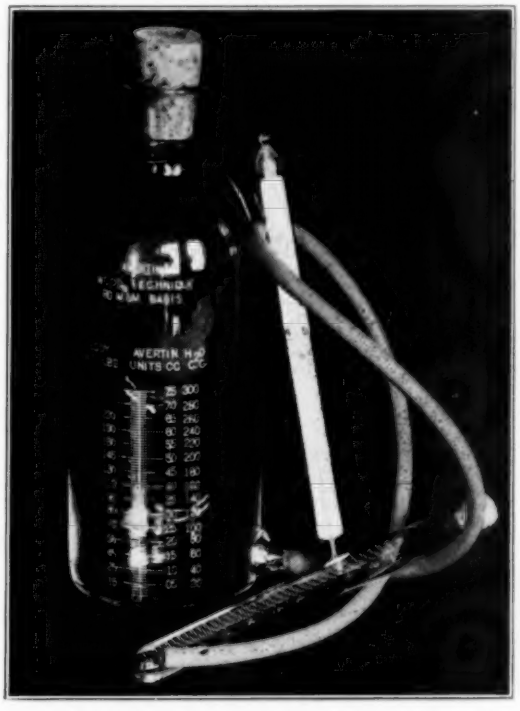


Fig. 1. Mixing flask; graduated test tube; 40°C special thermometer. (Wood. *J. A. M. A.*, 106: 276 [Jan. 25] 1936.)

In all types of operations including obstetrical procedures, avertin basal anesthesia has been successfully supplemented by most of the recognized anesthetic agents singly or in combination. The list includes ether, nitrous oxide, ethylene, cyclopropane and a few extremely exceptional cases in which chloroform was used. Local and spinal anesthetic agents also have been combined for avertin basal narcosis.

Avertin is a potent agent even in very small amounts. There is a wide margin of safety but carelessness in the measuring of single drops may make a noticeable difference. For teaching or clinical work exact readings are most important. This applies to both the amount of the avertin fluid used in the mixture and to the adjustment of the temperature of the water. The question of using ordinary tap water or distilled water has been settled in this series

of 2700 cases by a constant finding that tap water was satisfactory except in 3 instances. In these cases chemicals used in cleaning a boiler and joints of new pipes may have produced a chemical change in the tested solution. Every dose must be tested with Congo Red whether mixed with distilled or tap water. Tap water is suggested as it is heated or readily adjusted to the correct temperature. Where the source of the tap water and the use of chemical purificants are known there is reasonable safety in this departure from the manufacturers' published technique. Shipway stated that patients would be under- or overdosed by any standard table. This is true individually, but on an empiric clinical study of a large series it was found that a standard table could be established from which the anesthetist must use practical judgment in special cases.

The use of a definite scale based on weight as advocated by the manufacturer does not take into account age, sthenicity, circulatory stability, metabolism and emotional variation. The scale here proposed was presented a year ago, and has been subjected to one or two minor changes to be explained in detail. The original scale was developed from a graph of 1200 cases and this present report considers it in the light of 1600 additional administrations. There are three scales in metric proportions etched into the mixing flask of the avertin apparatus (Fig. 1). The legend, "80 mgm. basis" etched into the bottle, has caused considerable confusion. It does not mean that the amounts of avertin fluid used for the various weights is uniformly 80 mgm. per kilo of body weight. The scale etched on the bottle is derived from a curve, the highest point of which is 80 mgm. per Kilo and the lowest 46 mgm. per kilo (Fig. 2). The weight table etched in the left hand column is converted from kilos to actual pounds of body weight. The corresponding units of avertin fluid in cubic centimeters etched in the centre column of the bottle is based on the adjusted scale in such a way that the higher actual weight, the smaller milligram dose per pound is given. The third table etched in the flask shows the actual number of cubic centimeters of water at any given level. It is on the right side of the tables and is only to be used when the technique here described is not to be followed.

The weight scale showing actual pounds of body weight must be adjusted for age, metabolism and other factors previously noted. The adjustment is made in the amount of avertin fluid used in the mixture rather than on the pounds of body weight. For young persons, under ten years whose metabolic rate is relatively high, also for singers, alcoholics, athletes and hyperthyroids, the total amount of avertin indicated at the actual weight level is increased by one-tenth of the total amount of avertin indicated. It is not necessary to change the water level as this increase produces a concentration of 2.88 per cent instead of a 2.5 per cent solution. It has been found that concentrations as high as 3.5 per cent are non-irritating.

The second adjustment is for ages above fifty years. When one-tenth of the total dose of avertin fluid indicated has been deducted for each five years over fifty, satisfactory basal narcosis has followed unless the water level is adjusted but has proved satisfactory in this series of 2700 cases. In no patient, regardless of weight from 220 pounds and over, have we found it necessary to use more than 6.6 c.c. of avertin fluid to produce the desired basal narcosis. The basal narcosis sought by this technique is that amount of sedation which will permit the introduction of a pharyngeal airway without causing reflex or awakening the patient. Proof that the narcosis is actually light is obtained by manipulation of the airway against the walls of the pharynx which in most of these cases will produce gagging, coughing or awakening of the patient.

The final departure from the manufacturer's instructions for administration is the element of time. It has been observed

in the relatively normal patients, (whose systolic blood pressures are over 100 mm. Hg. and under 160), that they may receive the instillation of the total avertin dose as rapidly as it will flow from the flask held at 26 F. catheter length held above the rectum. For the patients whose blood pressures are below 100 or above 160, a slow instillation requiring approximately ten minutes has been found advisable.

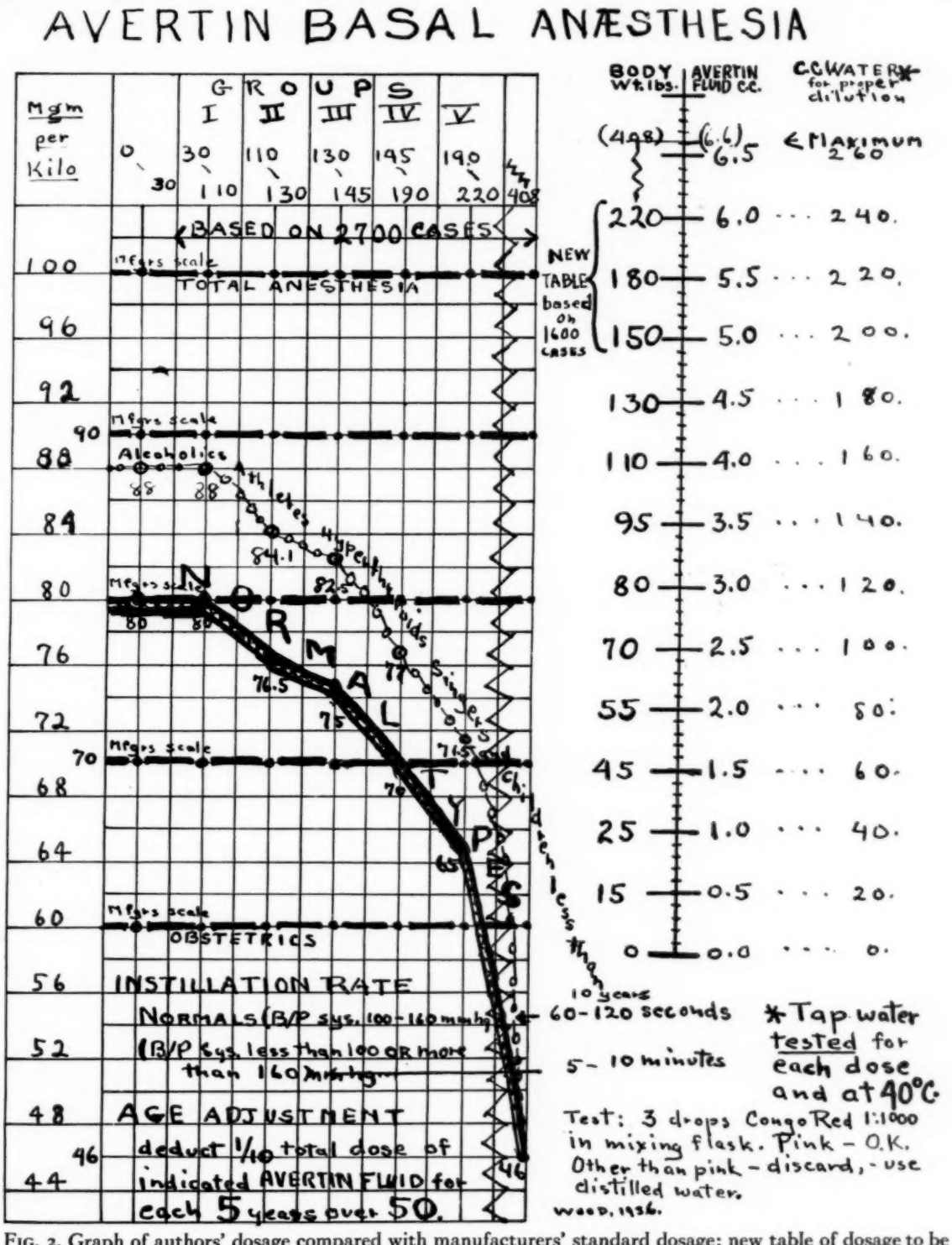


Fig. 2. Graph of authors' dosage compared with manufacturers' standard dosage; new table of dosage to be etched on mixing flasks.

When this technique is followed the drop in blood pressure in our series has not been greater than 23 mm. of mercury.

Fig. 3. Avertin apparatus. (Wood. *J. A. M. A.*, 106: 275 [Jan. 25] 1936.)

TECHNIQUE USING AVERTIN APPARATUS

Tap water is run into the flask up to the line indicated by the patient's actual weight in the left scale. The temperature of the water is then adjusted to exactly 40°C. On the center table is then read the number of cubic centimeters of avertin for the patient's "relative" weight. This amount is measured into the test tube and poured into the flask. It is necessary to add 0.2 c.c. of avertin fluid more than the indicated amount, as this amount adheres to the test tube. Three drops of congo red solution is added directly to the mixture in the flask, the cork stopper inserted, the delivery tube closed by catching it in the wire hook on the neck of the flask which is vigorously shaken two to ten seconds. This is necessary to produce a perfect mixture. The mixture will now be a milky pink and will be under slight pressure. The tip of the rectal tube is anointed with petrolatum and inserted into the rectum only far enough to permit free flow of the fluid. Petrolatum although a lubricant, is sufficiently sticky to prevent expulsion of the rectal tube by a nervous patient and is therefore preferred to other lubricants. The rate of injection is only as fast as the liquid will flow by gravity, the time consumed being usually less than ninety seconds. Should a fecal plug obstruct the flow, the flask is again stoppered and vigorously shaken. Owing to the expansion of the warmed alcohol in the closed container sufficient pressure is developed to expel the plug. Avertin should not be injected under pressure except in obstetric cases in which the normal flow may be obstructed by the natural processes.

The use of avertin in detail is as follows:

1. A cleansing enema is administered the night before the operation; no enema the morning of the operation. A mild sedative may be used the night before operation.
2. One and one-half hours before the operation is scheduled, morphine sulfate ⅙ gr. (0.01 Gm.) with atropine sulfate 1/150 gr. (0.0004 Gm.) is administered by hypodermic.
3. From thirty to forty-five minutes before the operation, avertin is administered by the technique described.
4. The patient should remain quiet in a darkened room for twenty minutes after the instillation of the avertin.

5. Immediately on return to bed, all patients having received this combination of basal narcosis and other anesthetic agent are given a hypodermic injection of 2 to 3 c.c. of a 25 per cent aqueous solution of pyridine-beta carbonic acid diethylamide (coramine). This is a routine procedure which has proved valuable as a prophylaxis against postanesthetic respiratory and cardiac depression occasionally seen prior to our use of this drug.

CONCLUSIONS

1. Avertin should be given by rectal installation for basal narcosis.

2. Avertin may be given in larger doses than for basal anesthesia for the control of certain specific conditions as tetanus, convulsions, delirium tremens, minor surgical procedures and dressings. It is especially indicated in certain types of surgery of the brain, thyroid and eye.

3. Avertin is contraindicated in all cases presenting renal or hepatic insufficiency that are classified other than mild.

4. A practical table and technique for the mixing and administering of avertin in a series of 2700 cases has been presented.

REFERENCES

1. The Winthrop Chemical Company, Inc. Avertin—basal Anesthetic.
2. Killian, Hans. The pharmacologic and chemical effects of avertin. *Zentralbl. fur Chir.*, 54: 1997–2003 (Aug. 6) 1927.
3. Eichholtz, F. *Deutsche med. Wchnschr.*, 53: 710, 1927; 55: 1537, 1929.
4. Shipway, Sir F. Selection of cases for avertin. *Brit. Jour. Anaestbesia*, 73 (April) 1930.
5. Kreiselman, Joseph. Avertin anesthesia; from the anesthetist's standpoint: A resume of eighteen months' experience. *Ann. Surg.*, 94: 885 (Nov.) 1931.
6. Bourne, Wesley and O'Shaughnessy, P. E. One thousand avertin anesthesias. *Can. Med. Assn. Jour.*, 31: 376 (Sept.) 1934.
7. Mueller, Lillian B. Report of 3000 cases of avertin anesthesia. *Jour. Indiana State Med. Assn.*, 29: 175 (April) 1936.
8. Wood, Paul M. Clinical use of cyclopropane and tribromethanol in amylene hydrate. *J. A. M. A.*, 106; 275 (Jan. 25) 1936.
9. Tannenbaum, Louis. Avertin anesthesia: resume of 150 cases. *Anesth. and Analg.*, 12: 15 (Jan.-Feb.) 1934.
10. Seevers, M. H., Waters, R. M. and Davis, F. A. The action of tribromethyl alcohol on the intraocular and intracranial veins. *Jour. Pharmacol. and Exper. Therap.*, 42: 270 (July) 1930.
11. Raginsky, B. B. and Bourne, Wesley. On several phases of the pharmacology of avertin. *Anesth. and Analg.*, 11: 33 (Jan.-Feb.) 1932.
12. Sebening, Walter. Recent researches and clinical advances in avertin narcosis. *Anesth. and Analg.*, 11: 145 (July-Aug.) 1932.
13. Bourne, Wesley and Raginsky, B. B. The effect of avertin upon the normal and impaired liver. *Am. Jour. Surg.*, 14: 653 (Dec.) 1931.
14. Morton, W. R. M. The effect of tribromethanol (avertin) on the electrical changes in the human heart. *Jour. Pharmacol. and Exper. Therap.*, 53: 137 (Feb.) 1935.
15. Scarff, John E. and Walker, Exum. Avertin and encephalography. *Jour. Nerv. and Ment. Dis.*, 83: 661 (June) 1936.
16. Bourne, Wesley, Bruger, Maurice and Dreyer, N. B. The effects of amytal and avertin on the blood, the temperature, and the functions of the liver and kidneys. *Can. Med. Assn. Jour.*, 24: 384 (Mar.) 1931.
17. Zucker, T. F., Newburger, P. J. and Berg, B. N. Influence of anesthesia upon pancreatic function. *Proc. Soc. Exper. Biol. and Med.*, 29: 294, (Dec.) 1931.
18. Bell, B. T. and Stokes, Joseph, Jr. The use of magnesium sulphate, avertin and sodium amytal with the Drinker respirator in the treatment of experimental strychnine poisoning. *Am. Jour. Med. Sc.*, 885 (June) 1933.
19. Stalberg, Samuel and Davidson, H. S. The newer treatment of strychnine poisoning. *J. A. M. A.*, 101: 102–105 (July 8) 1933.
20. Bernheim, B. M. and Taylor, R. A. Avertin in the pain crises of blood vessel spasm. *Ann. Surg.*, 99: 550 (Mar.) 1934.
21. Mitchell, H. S. Avertin as an auxiliary therapeutic measure in tetanus. *Can. Med. Assn. Jour.*, 32: 415 (Apr.) 1935.
22. Harrison, F. A. Three cases of tetanus: treatmen with antitoxin controlled by avertin. *Am. Jour. Dis. Child.*, 45: 445 (Feb.) 1933.
23. Boyce, Frederick Fitzherbert, et al. An analysis of mortality of gall-bladder surgery with an especial note on so-called liver death: 404 cases. *Surg., Gynec. and Obst.*, 63: 43 (July) 1936.
24. Heard, Kenneth M. Avertin in thyroid surgery: sixty consecutive cases. *Can. Med. Assn. Jour.*, 33: 395 (Oct.) 1935.
25. Saunders, F. W. and Narreau, O. F. Evipal and avertin in dental surgery. *Dental Cosmos*, 76: 967 (Sept.) 1934.
26. Looper, E. A. Tribromethanol as an anesthetic in operations on the nose and throat. *South. Med. Jour.*, 24: 238 (Mar.) 1931.
27. Editorial. Avertin Anesthesia as Viewed by the Patient. *Internat. Jour. and Surg.*, 48: 285 (July-August) 1935.

MORTALITY OF SPINAL ANALGESIA

BASED ON AN ANALYSIS OF 30 IMMEDIATE FATALITIES IN A SERIES OF 33,811 CASES*

J. Ross Veal, M.D., F.A.C.S. and Benjamin deKalb Van Werden, M.D.

NEW ORLEANS, LA.

THE story of spinal analgesia in American surgery begins in November, 1899, in the New Orleans Charity Hospital, with the unsuccessful attempt of Rudolph Matas to produce it by the use of eucaine B. A month later, Matas repeated the attempt using cocaine. This time he succeeded, almost too well, for the analgesia not only affected the lower extremities but also extended above the waist into the face and neck. He performed a hemorrhoidectomy with perfect ease, and his report of it a year later in the *Philadelphia Medical Record*, is, as he points out in a comprehensive paper on local and regional anesthesia, the first published record in America of an operation under spinal analgesia. His performance antedated by only a few days, he continues, a similar case reported by John B. Murphy of Chicago.

Matas' further experiences are interesting and illuminating in the light of the after history of this anesthetic agent. In no other case did the analgesia rise above the second lumbar vertebra, but in all succeeding cases, as in the first one, the usual reaction followed, chills, headaches, vomiting and pyrexia. The analgesia was so admirable, however, that he continued to use the method and he was on the point of reporting his first 50 cases with it when he was halted by three untoward happenings, a respiratory collapse that just escaped a fatal outcome, a hyperpyrexia of 104°F., and an intense rachialgia and headache that persisted for months. These accidents, as he writes, not only postponed the report but "made me realize that the dangers of spinal anesthesia with cocaine could not possibly be compensated by the simplicity of the technique nor the effectiveness of the anesthesia." In 1905–1906, after the introduction of novocaine by Braun, he resumed its use, but always tentatively, never again to exceed the limits of the twelfth dorsal or the first lumbar space, and always with strict regard for its indications and limitations. So carefully did he employ the method that in 1927, when he resigned his active connection with Charity Hospital, he had used it, he reports, in only 232 operations, including the cases in his private practice.

In decided contrast to the limited and cautious use of this method by the man who was the first to employ it there, spinal analgesia is now used in the New Orleans Charity Hospital more extensively and probably more frequently than at any other institution in America. In 1926 Graffagnino was able to report 7322 instances of its use, and in the eleven and a half years which this present study covers it has been used in 33,811 cases. In 1925, 1165 operations were done under spinal analgesia. The present average is about 5000, which represents approximately 50 per cent of all the general surgical cases, and its use is now routine or almost routine on many services.

The routine use of any anesthetic agent immediately suggests certain generalizations which verge on the critical, it is true, but which are none the less entirely fair. In the first place, under such circumstances there is obviously little if any individualization of cases; the patient and his needs, his disease and its necessities, are almost automatically subordinated to the routine of the service. In the second place, the routine use of any method almost inevi-

* From the Departments of Surgery of the School of Medicine of Louisiana State University, and Charity Hospital in New Orleans.

tably makes for indifference if not for actual carelessness. An interne, inexperienced and untrained, at first is permitted, and shortly is expected to administer the anesthesia, and it is but natural that he should with equal promptness lose most if not all of his respect for its risks. The surgeon, furthermore, because the anesthesia is usually so satisfactory, tends to forget the state of the patient, even when that state happens to be precarious, and there is, unfortunately, seldom any systematic observation of his condition by a person who has that responsibility and no other in the operating room. In the third place, the routine use of any anesthetic agent is likely to result in a relaxation, if not in an entire disregard, of the postoperative precautions that contribute so largely to its safety. Finally, the surgeon and his assistants, as their skill and experience with it increase, are more and more likely to forget that they are dealing with an agent which, when once administered, cannot be withdrawn, and the untoward effects of which when once they have manifested themselves, can be combatted only by measures which are entirely symptomatic and often ineffective. These criticisms are perfectly fair when spinal analgesia is used routinely, and the fact that only a small proportion of cases terminate fatally does not in the least detract from their application to all cases.

The *total mortality of spinal analgesia* is very difficult to estimate. In a fair proportion of all cases there is a delayed hospital mortality; in another group this type of anesthesia is responsible for only part of the fatal outcome; in a small proportion of cases there is a remote mortality. These considerations, however, we have chosen to disregard and in this study we are confining ourselves to the direct, immediate mortality of spinal analgesia, which is represented by 30 fatalities in the 33,811 cases in which it was used in the New Orleans Charity Hospital between January 1, 1925, and July 1, 1936. All of these deaths occurred in the operating room, immediately or shortly after the anesthetic had been administered, and there can be no question as to the responsibility of the mode of anesthesia for the fatality which followed its use.

We note, first, a marked difference in the mortality rates for the first five years of this study as compared with the last six and a half years. In the first period, which ended in 1929, there were 3940 spinal analgesias with 6 deaths, or 1 in every 656 cases. In the second period, which ended July 1, 1936, there were 29,871 spinal analgesias with 24 deaths, or 1 in every 1244 cases, one-half the mortality of the first period. The standardization of technique and the use of less toxic agents, chiefly novocaine, are responsible for the decrease. It is partly explained, too, by North's pertinent comment that the mortality of spinal analgesia does not really represent its risk, but represents, rather, the acquisition of experience, and as such approximates the risk still assumed by the average surgeon whose training is satisfactory but the number of whose cases is relatively small.

We have always felt strongly that spinal analgesia is not a method to be employed on very young children, and we feel even more strongly that it should not be employed on aged subjects. This study confirms that point of view. In the 30 deaths the age range was between seven and eighty years, but 9, or very nearly one-third of the total number, occurred in persons above sixty years of age, although surgery is done infrequently at this time as compared to its performance in younger subjects.

The sex incidence, 18 males to 12 females, needs no extended discussion, but the racial incidence introduces different considerations. The proportion of Negro to white hospital admissions varies with the years, but the average is approximately 45 Negro to 55 white admissions. It seems more than accident, then, that 21 of the 30 deaths, or more than two-thirds, occurred in Negro patients. There are several possible explanations. The Negro is very

often a poor surgical risk; his tendency is to ignore "inaugural symptoms"; his mode of life is unhygienic and frequently he is the subject of advanced organic disease, particularly of the cardiovascular variety. Whatever the reason may be, he is obviously a less good risk for spinal analgesia than is the white patient.

All but 4 of the 30 deaths occurred with the use of novocaine. Two of the 4 occurred with tutocaine (1.5 grains each) and 2 with apothesine (65 and 120 mg., respectively). In the novocaine group 5 deaths occurred with doses above 150 mg. (2 with 180 mg., 2 with 200 mg. and the other with 300 mg.), and it is clear that the risk increases with the size of the dose. On the other hand, in 21 cases the dosage was 150 mg. or less, which is not an excessive or even a particularly large dose. There is still no method of determining before the catastrophe the tolerance of the individual organism to cocaine and its derivatives, and until this point can be determined, there seems no doubt that certain fatalities will continue to occur as the result of a dose not excessive in itself but apparently too large for the particular individual to whom it is administered.

Individual tolerance to dosage may still be a matter of conjecture, but it is always a fairly simple matter to evaluate the individual patient as a surgical risk. Certain individuals, because of the inherent seriousness of their local disease, or because of its advanced state, or because of their associated constitutional diseases, or for all three reasons, are poor risks for any sort of anesthesia. These circumstances are all exhibited in the fatalities we are studying.

Eighteen of the 30 deaths, as the appended chart shows, occurred in abdominal conditions which were intrinsically serious and most of which were rather far advanced (intestinal obstruction, peritonitis, gunshot wounds, in which hemorrhage is an additional factor of risk, and amebic abscess of the liver). Three others occurred in patients who had serious diseases and in whom operation was serious but who were not necessarily poor risks for that reason (cholecystitis, carcinoma of the stomach and gastroenteritis with ileus). An operation for popliteal aneurysm is always one of considerable magnitude, particularly when, as in this case, hypertension introduces an additional risk. Patients with prostatic hypertrophy and carcinoma of the urinary bladder often are poor risks at Charity Hospital because they frequently exhibit an advanced type of pathology. A patient with urethral stricture associated with extravasation of urine is always in poor condition. It is clear, then, that most of these deaths occurred in persons who were poor or doubtful risks and some of whom had associated conditions which added to the gravity of their state.

The 3 patients with uterine fibroids deserve special mention. They were all Negro women; 2 were thirty-one and one was thirty-four years of age. They were all presumably good surgical risks, though whether they were good risks for spinal analgesia is another matter; it must be remembered that uterine fibroids of any special size always introduce an element of risk because of the sudden change of intra-abdominal pressure which follows their removal. We have seen experienced gynecologists in this institution take half an hour or longer to suction out the contents of a large ovarian cyst in order to avoid this very risk, a precaution that is impossible, of course, with solid tumors. North comments on this danger, mentioning his own experiences in a case of ascites and another of ovarian cyst, and citing, too, the "birth shock" described by certain German authors as due to this cause. His point is well taken, that the compensatory circulatory changes which are necessary under such circumstances may not be possible under the handicap of spinal analgesia.

It should be noted, too, that one of the patients with uterine fibroids was obese, as were several other patients in the group of deaths. The obese patient should be

viewed with respect as a candidate for all surgery, and the difficulties and dangers of hysterectomy in a short, stout Negro woman with a deep pelvis can be fully appreciated only by those who have performed the operation under such circumstances. In 2 instances the dosage of novocaine was 200 mg., which is high though not excessive. Another of these patients suffered from hypotension, which would make her, in our opinion, a doubtful candidate for spinal analgesia.

30 DEATHS FROM SPINAL ANALGESIA

No. Cases	Diagnosis	Obesity	Hypertension	Hypotension	Hemorrhage
9	Intestinal obstruction	3	2	1	
6	Peritonitis	..	..	1	
3	Uterine fibroids	1	..	1	
2	Gunshot wounds of abdomen	1	1	..	1
2	Acute appendicitis	1			
1	Chronic cholecystitis	..	1		
1	Amebic abscess of liver				
1	Gastroenteritis and ileus				
1	Carcinoma of urinary bladder				
1	Urethral stricture and urinary extravasation	..	..	1	
1	Carcinoma of stomach				
1	Popliteal aneurysm	..	1		
1	Hypertrophy of prostate				
30	Total	6	5	4	1

Any abnormality of the blood pressure, whether of the hypotensive or the hypertensive variety, introduces an element of risk in a type of anesthesia with which a sudden, sharp fall in blood pressure is likely to be associated. The very fact, says Matas, that various types of vasostimulants must still be administered simultaneously with the spinal injection is the best proof that bulbar paresis and arterial hypotension still remain as potential and unpredictable dangers. Potential and unpredictable the danger may be in the normal patient, but the danger is obvious in the abnormal one, and the surgeon who uses spinal analgesia in patients with hypotension and hypertension is courting disaster for them and for himself.

It is an admitted fact that every variety of anesthesia will result in an occasional unexpected fatality, no matter how carefully it is given or how good the risk may seem to be. But it is equally fair to say that the indiscriminate, routine use of any type of anesthetic agent will result in considerably more than the occasional, apparently inevitable death. Spinal analgesia is easily administered and rapidly effective, and many times its contraindications can be ignored with impunity. But frequently they cannot be, and every surgeon who uses it ought to bear in mind that he is dealing with an agent which, when once given, cannot be withdrawn. His own time and convenience, which too often are the chief indications for its use, can scarcely be set against the risk to human life which spinal analgesia always entails when it is used in cases in which contraindications exist.

Various studies have proved that the method is contraindicated in abnormalities of the blood pressure, both of the hypertensive and the hypotensive variety, in obese patients and it should be used with extreme caution in acute abdominal disease which has progressed to the point in which toxemia and shock, both vasodepressant states, enter the picture. It is obviously unsuited for surgery in young children, and these figures show that it is even more definitely unsuited for surgery in aged subjects. The fact that the mortality from spinal analgesia in these 33,811

cases was only a fraction of 1 per cent is not the point at issue, but that a more careful selection of cases will reduce that mortality still further, so that the mortality of spinal analgesia will more closely approximate the rate of inhalation anesthesia.

Matas wisely concludes his discussion of this subject in these words:

> As long as we are dealing with a method that is capable of blocking the most vital conducting functions of the cord and medulla, which differs from all other neuroregional blocks by its liability to widespread and uncontrolled diffusion from the primary seat of injection, we should confine its use to the special indications and limits which a large and growing experience has demonstrated to be relatively safe. . . . Personally I regard spinal anesthesia as the supreme attainment of regional anesthesia, but I do object to the routine, indiscriminate and wholesale use to which it has been put in many quarters.

SUMMARY

A study of the mortality of spinal analgesia at Charity Hospital in New Orleans over a eleven and a half year period, is presented. The analysis includes 33,811 cases in which spinal analgesia was used. This study is primarily concerned with the fatal cases in this series.

The contraindications for the use of spinal analgesia are discussed.

REFERENCES

Graffagnino, P. Spinal anesthesia. *New Orleans Med. and Surg. Jour.*, 79: 657–667 (March) 1927.

King, O. C. Spinal analgesia. Report of 1500 cases. *Ann. Surg.*, 101: 690–701 (Feb.) 1935.

Matas, R. Local and regional anesthesia with cocain and other analgesic drugs, including the subarachnoid method, as applied in general surgical practice. *Philadelphia Med. Jour.*, 6: 820–843 (Nov.) 1900; Local and regional anesthesia; a retrospect and prospect. *Am. Jour. Surg.*, 25: 362–378 (Aug.) 1934.

North, J. P. Use and abuse of spinal anesthesia. *Ann. Surg.*, 101: 702–707 (Feb.) 1935.

A NEW APPARATUS FOR ARTIFICIAL RESPIRATION

SOME COMMENTS

WILLIAM BRANOWER, M.D.

Mt. Sinai Hospital

NEW YORK

WHEN is a person dead? The answer of one physiologist was "When it can be definitely proved that he is not alive." The burden of proof is on the side of life, and that proof cannot always be so readily established. The great tenacity to life of individual cells and organs of the body has been demonstrated in the laboratory. The physiological experiment in which the excised heart of an animal is stimulated to beat for some time is well known. It has often been noted that the heart of a patient will continue to beat for several minutes after respirations have ceased. In all cases of asphyxia, therefore, it should be assumed that life still exists when all evidence seems to point to the contrary. Adequate measures must be instituted to revitalize, if possible, the all but completely paralyzed respiratory, cardiac and other vital centers.

Artificial respiration is one of the most effective measures of resuscitation. To demonstrate the effect of artificial respiration on the failing heart due to asphyxia, the writer performed the following experiment upon a living dog under anesthesia. The sternum and part of the ribs were resected, exposing the heart and lungs. The double pneumothorax thus created tended to collapse both lungs. Artificial respiration was then established. The respiratory excursions of the lungs and the active heart beats were visible. Artificial respiration was then interrupted to permit the lungs to collapse for periods ranging from five to eight minutes. The heart which at first was beating vigorously and rhythmically was then observed to be gradually failing. At the end of the eight minute period during which the lungs were almost completely collapsed, the heart was still contracting feebly from time to time. When artificial respiration was reestablished, the full inflation and deflation of the lungs revitalized and stimulated the heart to resume its normal forceful contractions. A motion picture of this experiment is on record.

Success or failure to resuscitate a victim of asphyxia depends upon the degree of asphyxia and the technique employed. The degree of asphyxia is proportionate to the potency of the asphyxial agent and to the extent of the trauma which that agent inflicts upon the brain, the respiratory, cardiac and other vital centers.

Effective artificial respiration depends in great measure on the technique employed to ventilate the lungs successfully. The questions arise: What volumes of resuscitative gases and what intrapulmonary pressures are essential, and how do some of the measures and apparatus employed for artificial respiration meet the requirements for effective ventilation of the lungs?

Under normal conditions there is an exchange in the average adult of approximately 500 c.c. of air during each respiration. This tidal volume of air can be augmented threefold by a voluntary deep inspiration, i.e., by 1500 c.c. of complementary air. By a voluntary forced expiration after a normal quiet inspiration, a supplemental volume of 1500 c.c. of air can be exhaled. The vital capacity of the average adult lungs is therefore about 3500 c.c. The full lung capacity includes the stationary volume of air of about 2000 c.c. or a total of about 5500 c.c. These figures indicate the large volumes of air exchanged during voluntary deep breathing.

In extreme cases of asphyxia, with respirations at a standstill and the vital

centers in the medulla almost completely paralyzed, insufflation of small volumes under low pressures may not suffice to inaugurate that chain of stimuli which motivates the respiratory mechanism. Bolder methods must be employed. Two or even three times the normal tidal volume may be necessary and may be insufflated without danger.

The intrapulmonary pressure, which normally varies from approximately minus 3 mm. of mercury at the end of a quiet inspiration to approximately plus 3 at the end of a quiet expiration, may be raised with these extra volumes to as much as plus 20 mm. or more of mercury.

The prone pressure method of artificial respiration is used extensively with reported success. By actual measurement this method cannot effect a respiratory exchange of more than 350 c.c. per respiration, which is less than the normal tidal volume. Nature has liberally provided normal life with "factors of safety" which account for the survival of many patients, no matter what resuscitative technique is employed. Any method of artificial respiration or any apparatus for that purpose is sufficient. In extreme cases of asphyxia what hopes of success can be entertained of resuscitating a victim just this side of the threshhold of life by providing less than the normal tidal volumes per respiration?

Successful resuscitations are also reported by use of various inhalers, which rely upon inhalation of resuscitative gases contained in a resilient bag. In extreme cases of asphyxia, sufficient pressure to inflate an atelectatic lung cannot be developed in a resilient bag even at its maximum inflation.

Any apparatus used for artificial respiration should be equipped to deliver at each inspiration ample, measured and controlled volumes which will inflate the lungs to the desired capacity within safe and adjustable pressure limits.

The apparatus devised by the writer was designed to deliver either the tidal volume or double and triple the tidal volume with each inspiration, to indicate visibly the intrapulmonary pressure at all times and to safeguard against excessive intrapulmonary pressure.

A full description of the apparatus appeared in a previous publication.* In essence it is as follows:

It is a light portable apparatus which can be instantly put into use. It can be used with any size medical or commercial cylinder containing oxygen, carbon-dioxide and oxygen, or with air if other resuscitative gases are not available. It incorporates the features described below:

A. A manifold and three yokes to receive the cylinders containing various resuscitating gases.

B. A pressure gauge in the manifold to indicate the available supply of gas in any one cylinder. Shut-off valves permit the installation of fresh supply cylinders without interfering with the resuscitative measures.

C. An air inlet guarded by a stopcock permits the use of air from any source in the absence of other resuscitative gases.

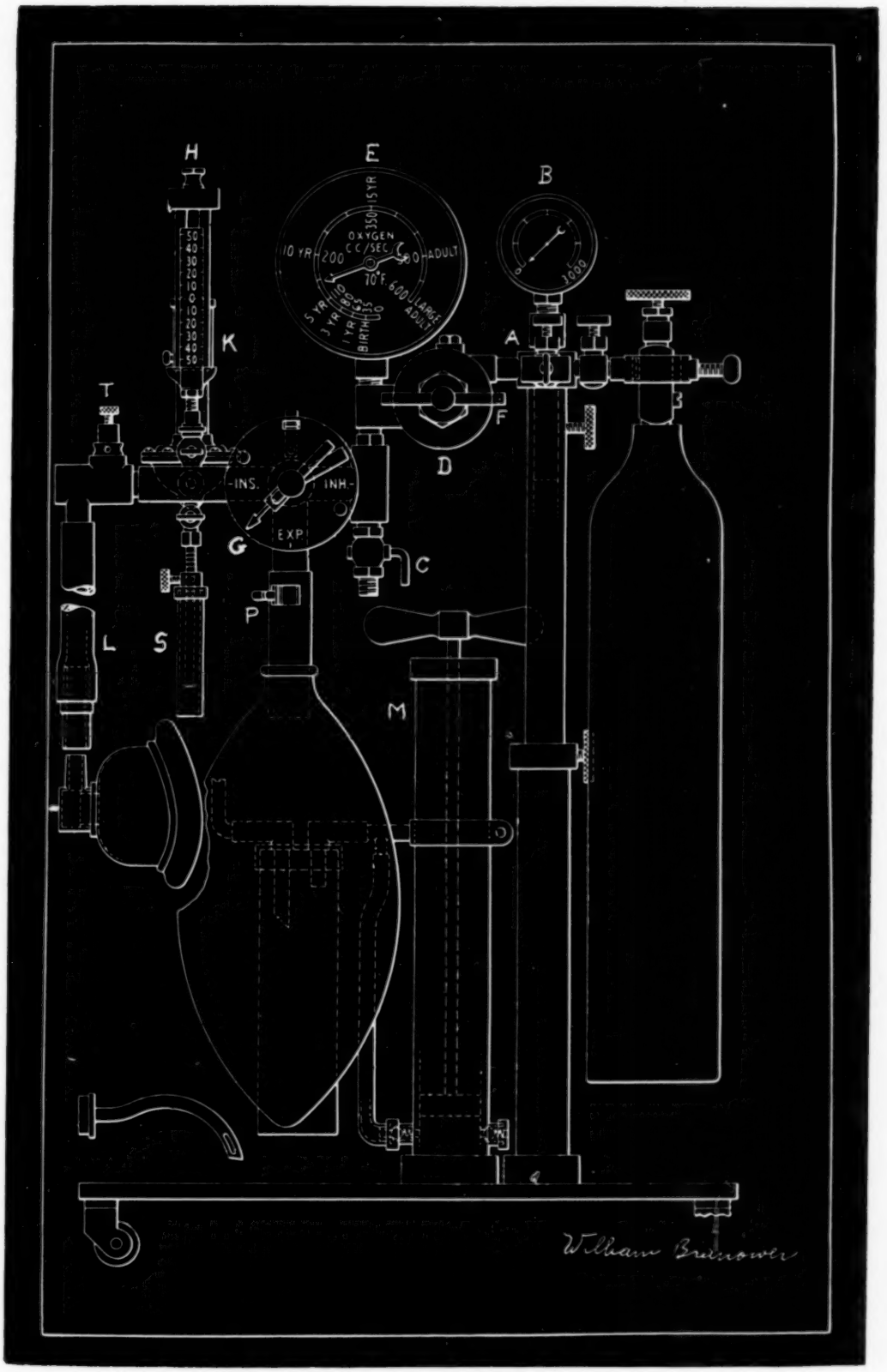
D. A pressure regulator and reducing valve can be set by the control valve F to deliver from 35 to 600 c.c. of gas per second. These figures represent the various tidal volumes breathed by different age groups per inspiration. By means of the respiratory valve described below the inspiratory phase can be made to last two seconds in which time double the tidal volume will be delivered, or three seconds when triple the tidal volume is desired.

E. A dial surmounting a flow gauge indicates the amount to be delivered per inspiration for various age groups.

F. A control valve regulates the volume flow per second.

G. A respiratory valve which is under complete control of the operator regulates the rate and rhythm of the respirations and the amplitude of each inspiration. It is capable of three important positions which

* Branower, William. Artificial respiration by an apparatus which permits measured and controlled volumes and pressures. *Jour. Thoracic Surg.*, 5: 377–384 (April) 1936.



Branower Apparatus for Artificial Respiration.

are indicated by a pointer. The inspiratory position permits the resuscitating gases to flow from the apparatus direct to the patient without an intervening bag. The expiratory position shuts off the supply to the patient and permits the expired gases to escape into the open air. The inspiratory phase is an active process on the part of the machine and the operator, who aims to inflate the lungs to the desired capacity and pressure; the expiratory phase is passive. Any suction to facilitate expiration is unnecessary, even dangerous, and one intentionally dispenses with it. The natural high elasticity and resiliency of the lungs affect the immediate recoil to the collapsed state when the pressure or inflating force is removed at the end of the inspiratory phase. The inhalation position is used only when there are reflex or natural respirations, and permits to-and-fro respirations of any therapeutic gases from a bag. The extent of rebreathing is regulated by an expiratory valve, *T*. A butterfly air vent, *P*, at the entrance to the bag permits respirations of air.

H. A manometer on the patient's side of the respiratory valve indicates the intrapulmonary pressure at all times.

K. A large dial safety valve on the patient's side of the respiratory valve automatically blows off when the intrapulmonary pressure exceeds the safety limits. The relief valve can be adjusted to blow off at various pressures, from 5 mm. to 20 mm. or more of mercury. As a further precaution against the danger of excessive intrapulmonary pressure a second safety valve, *S*, is incorporated. This is of the mercury type and can also be adjusted and set to blow off at various pressures.

L. A delivery tube connects the apparatus with the patient. It is short (to eliminate dead space), flexible, noncollapsible, and of large lumen, which permits to-and-fro breathing without resistance. The tube ends in an adapter which fits a face mask, a pharyngeal airway, or an intratracheal tube.

M. A suction pump and receptacle. This is an independent manually operated unit used to clear the mouth and air passages of obstructing fluid or semifluid material. At no time should this suction be used as an aid to expiration.

The apparatus is adapted for use either by intratracheal insufflation or by face mask. The former is undoubtedly the most effective method. But artificial respiration to be of value must be instituted instantly. Unfortunately, however, when the emergency arises, the services of a physician skilled in intubation are rarely available and resort to a simpler technique must be taken. Delivery of resuscitative gases through a well fitting face mask is very practical because the method can be easily applied by a lay rescuer, who is usually first on the scene.

When intratracheal technique is employed the catheter must be made to fit snugly within the trachea, otherwise the gases will escape alongside the tube without inflating the lungs. When a face mask is used, inflation and overdistention of the stomach must be avoided either by pressure upon the epigastrium or by the insertion of a stomach tube. An airway which can be easily introduced, even by a layman, before the mask is applied, will prevent intraoral obstruction by the falling back of the tongue.

This apparatus is presented in the hope of making a further contribution to the technique of resuscitation by artificial respiration.

NEW INSTRUMENTS

A SPECIAL SYRINGE FOR USE IN SPINAL ANESTHESIA

TECHNIQUE IMPROVEMENT

GEORGE SANFORD FOSTER, M.D.

Surgeon to Lucy Hastings Hospital

MANCHESTER, NEW HAMPSHIRE

WE have observed in numerous surgical clinics as well as our own that there remains the possibility of air as well as direct contact contamination in the administration of spinal anesthetics.

It would seem that it is still one's duty, as well as one's desire, to perfect any technique in surgical procedures to the point of ultra-minimum possibility of contamination in the slightest degree.

With this end in view we have attempted to construct a syringe which will permit the securing of the spinal fluid, dissolving the crystals or admixing the solution of the anesthetic in either case, with the spinal fluid without any possibility of contamination.

This is accomplished by eliminating all extra moves and any unnecessary disconnecting or reconnecting with the spinal needle.

In other words with this special syringe the anesthetic of choice can be readily dissolved and mixed with the spinal fluid all in one move minus but one disconnecting, as well as eliminating any conveying from one point to another. Thus is the administration of the spinal anesthetic made very simple and its accomplishment accurate and efficient.

DESCRIPTION OF SYRINGE

The instrument is in reality made up of two connected units *A* and *B*. Unit *A* is a graduated glass barrel of 5 c.c. capacity, 1. The lower end of this glass barrel is harnessed by a circular band flange, 2. The tip of this flange, 3, is a standard connection for spinal needles. Division, 4, is a blind cap which fits over Unit *A* connection when disconnected from the spinal needle.

Running at an angle from the flange, 1, is a second connection, 5. This connection is standard for the ordinary hypodermic needle. The final division of unit *A* is a triple loop grip, 6, which is constructed of metal. The two lateral loops admit the index and middle fingers of the hand while the thumb is introduced through the top or middle loop which controls the metal piston and plunger. Thus Unit *A* is described as to its divisional construction assembled and disassembled.

Unit *B* is the ordinary hypodermic syringe 30 m. capacity with its two divisional segments, the barrel and piston, 7 and 8, respectively.

TECHNIQUE

Both Unit *A* and *B* are disassembled and dry sterilized in packet in the autoclave. This is done to prevent any accumulation or condensation of moisture either on the outside or inside of the plungers and barrels.

During the preparation in the operating room the sterile nurse places the crystals or solution of the anesthetic within the barrel of unit *B*. The plunger is then set in place and unit *B* connected with unit *A*. The anesthetist then follows his usual technique in introducing the spinal needle and securing the tap.

Immediately the tap is secured the blind cap is removed from Unit *A* and contact made with the spinal needle. The anes-

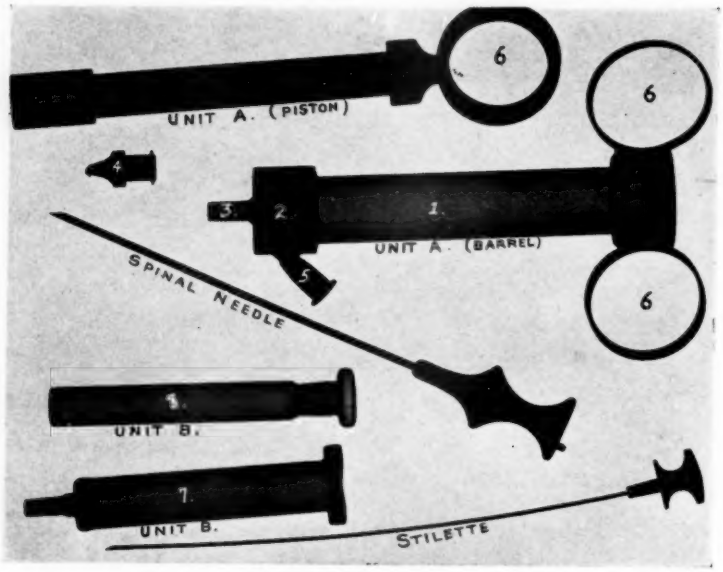


FIG. 1. Units A and B disassembled.

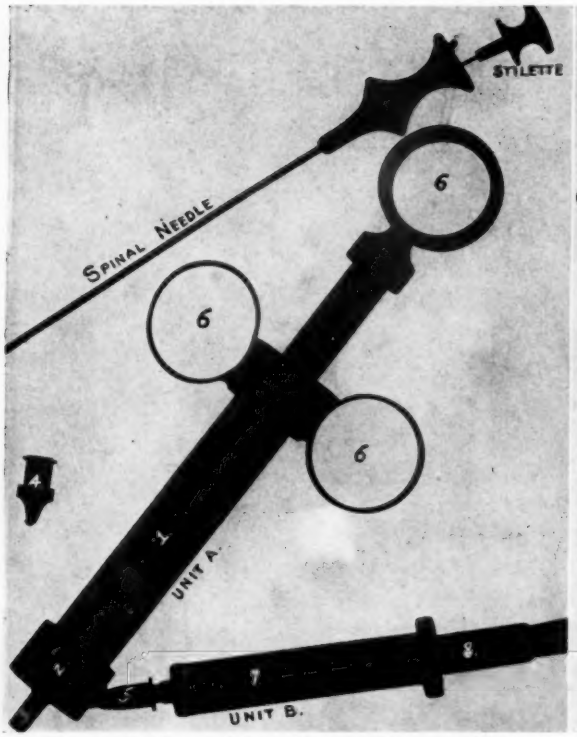


FIG. 2. Syringe with units A and B assembled.

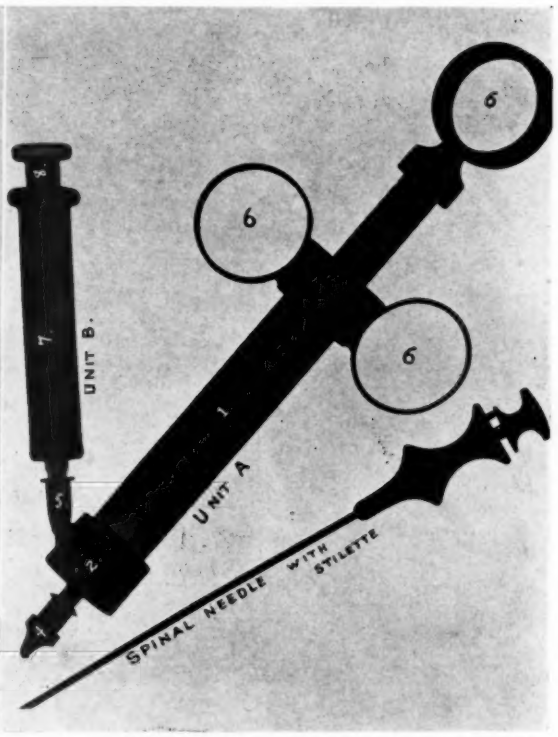


FIG. 3. Units A and B with pistons of each partially withdrawn.

thetist's fingers then engage the triple loops and the plunger of Unit *A* is very slowly withdrawn until the desired amount of spinal fluid is in the barrel of Unit *A*.

Unit *A* is then disconnected from the spinal needle and the stilette temporarily replaced and the blind cap replaced over the nipple of unit *A*. The plunger of unit *A* is then slowly forced downward, permitting the spinal fluid to run from the barrel of unit *A* into the barrel of unit *B*. This procedure will automatically force the piston and plunger of unit *B* upward.

As the lower end of the plunger of unit *B* reaches the 30 m. point the plunger of unit *A* is then withdrawn slowly from the barrel of unit *A* and this procedure will draw the plunger of unit *B* downward.

When the lower end of the plunger of unit *B* reaches 10 m. point, the piston and plunger of unit *A* are again slowly forced downward until the lower end of the plunger of unit *B* again reaches the 30 m. point. This procedure is repeated slowly two or three times or until the crystals in the barrel of unit *B* are dissolved completely. When this is accomplished the piston and plunger of unit *A* are again withdrawn slowly until the plunger of unit *B* reaches the bottom of the barrel of unit *B*. The plunger of unit *B* is then held in this position with the thumb of the left hand, and the blind cap removed from the tip of unit *A* and unit *A* again connected with the spinal needle following the removal of the stilette. The piston and plunger of unit *A* are then forced slowly to the bottom of the barrel of unit *A*, then slowly withdrawn again to the 3 c.c. point and again slowly forced to the bottom of the barrel. Thus the anesthetic fluid becomes thoroughly admixed with the spinal fluid and the spinal needle withdrawn without disconnecting from unit *A*.

The withdrawal or introduction of either piston will, without contacting the other piston, automatically control the one not contacted so that it moves in the opposite direction to the controlled or contacted piston.

This contrivance has materially simplified the technique of spinal anesthesia and minimized the liability of contamination or break in asepsis.

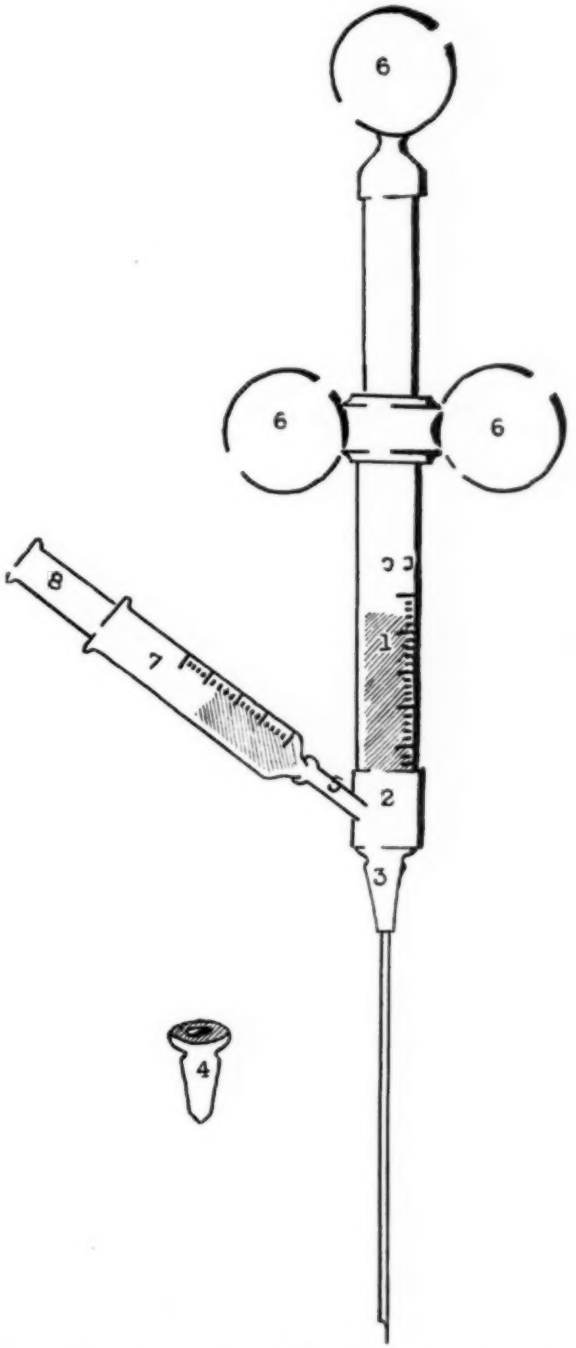


Fig. 4. Units A and B assembled and ready for use: 1, graduated barrel; 2, circular band flange; 3, tip of flange; 4, blind cap; 5, standard connection for hypodermic needle; 6, triple loop grip; 7, ordinary hypodermic syringe; 8, piston of ordinary hypodermic syringe.

ELIMINATION OF UPPER ABDOMINAL DISTENTION BY CONTINUOUS ASPIRATION DURING OPERATION

GERALD H. PRATT, M.D., F.A.C.S.

Instructor in Surgery, New York Post-Graduate Medical School of Columbia University

NEW YORK CITY

THE use of the principle of suction siphonage by inlying duodenal tube after an abdominal operation has become quite general and at many clinics is a routine procedure. The work of Wangensteen and others has been instrumental in standardizing the procedure. Several apparatus have been devised for the purpose, nearly all based on the underlying principle of the suction created by the effort of a fluid in an inverted elevated container to pass to a container at a lower level.

During operations on the upper abdomen, particularly the stomach, duodenum and gall bladder, surgeons have been annoyed by the protrusion or "flopping around" of the distended stomach and small intestine, caused frequently by the effort of the patient to gag, vomit or strain. We have shown that nearly all of this distention is swallowed air. This makes the operation technically more difficult and at times actually hazardous. It is particularly troublesome when anesthesia is incomplete or wearing off, as in local or spinal anesthetics, or with the violent breathing of a patient who takes the inhalation anesthesia poorly. At times, the organs become so distended that vision is impossible, and anesthesia must be carried to a dangerous point or the operation even terminated.

After considerable experience with suction siphonage in all its forms, it was decided to see if the suction would aid us in overcoming this distressing operation problem. The duodenal tube was placed through the nose and the suction kept open throughout the operation. We were surprised to note the ease with which the distention of the viscera could be eliminated and the decompression maintained. The stomach could be entirely flattened and the air, gas, regurgitated bile and saliva evacuated as rapidly as collected. It is advantageous even when the stomach has been carefully prepared by gastric lavage, as the nervous excitation, the vomiting reflex, and crying or swallowing of air will distend the stomach. In our gastric work we prepare the stomach with a lavage of diluted hydrochloric acid solution, leaving some of this solution in the stomach until we are prepared to open the organ. At that time we evacuate the fluid by opening the suction-siphonage system. Gastric lavage on the operating table can be easily effected in this way.

While on the Babcock Surgical Service at the Temple University, a standard apparatus was devised by the author for the purpose of decompression. This apparatus has the added advantage of being a portable single unit, easily controlled by the nurse, attendant or anesthetist. (Fig. 1.) This evacuator has been partially described elsewhere, but in brief utilizes the previously mentioned principle of hydraulic suction with the additional feature that the water jugs can be changed at will without disturbing the set or the patient. When one jug is empty it is lowered and the other one rises while a three-way valve controls the center or collecting jug. A burette for irrigation of the duodenal tube by way of a "Y" tube is kept clamped off when not in use.

The surgeon, who has spent time valuable to the patient and nervous energy important to himself, in efforts to protect his field from the distended viscera with traumatizing packing and retractors, will be surprised at the ease with which this

difficulty can be surmounted. The small tube through the nose in no way interferes with the anesthetist if a general anesthetic is used, and with the suction open regurgitation of the tube is nearly impossible. At the end of the operation the tube may be left in place and a secondary distention prevented by aspiration at indicated intervals.

With distended gall bladders which we desire emptied before their removal, without the contamination of the aspirating needle, we have been able with the abdomen open to place the tip of a nasal duodenal tube in the second portion of the duodenum, and with the suction applied to collapse the gall bladder by drainage through the common duct. Where the stone is impacted tightly in the neck, it is sometimes possible to work it back manually into the gall bladder, and then drain the gall bladder contents into the duodenum with the suction, thus eliminating a possible peritonitis from a leaking puncture hole. We are continuing our experiments along this line at the present time.

It is the suggestion, therefore, that surgeons working in the upper abdomen anticipate this distention factor by inserting the inlying duodenal tube before operation and having a suction siphonage device at hand ready for use. It is our experience that this suggestion will be a welcome addition to the routine preparation.

SUMMARY

1. An aid in eliminating the distention factor during an abdominal operation is described, using the author's modification of the Wangensteen type of suction siphonage.

2. The Pratt evacuator is briefly described.

3. The efficacy of the evacuation in gastric work is stressed.

4. The value of the procedure in operations upon the biliary tract in the presence of a tightly distended gall bladder is outlined.

5. The routine insertion of a duodenal tube prior to operation and the attachment of an evacuation apparatus for continuous decompression during surgical procedures on the upper abdomen is advocated, and a plan for gastric lavage just prior to the opening of the stomach by this same method is presented.

Fig. 1. The Pratt evacuator in use during an operative procedure.

SIMPLIFIED METHOD OF DRAWING BLOOD FOR CITRATE BLOOD TRANSFUSION*

H. D. COGSWELL, M.D.

INDIANAPOLIS, IND.

MANY methods have been devised to draw the donor's blood for citrate blood transfusions but some have been too complicated to be practical and most of the other means have some undesirable features.

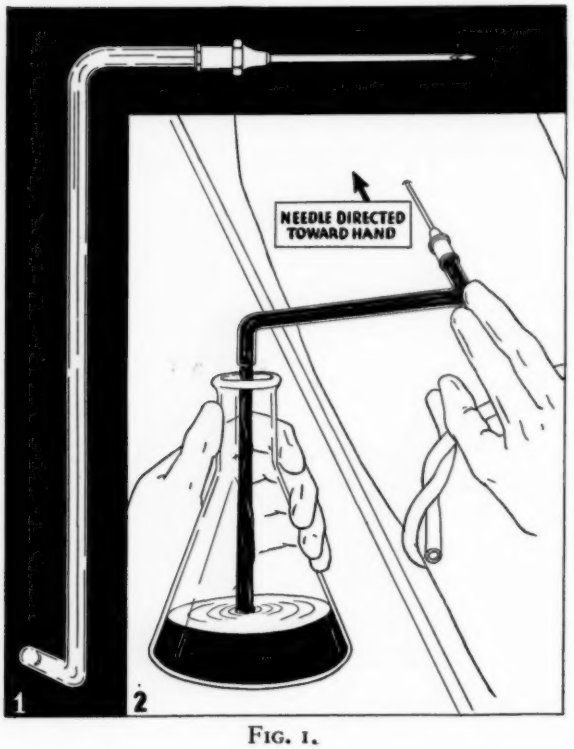


FIG. 1.

Numerous procedures in drawing blood have been used, including the multiple syringe method, Kempton-Brown tubes and a suction apparatus requiring much rubber tubing. In most instances these have been successful, but on occasions all methods have failed to perform satisfactorily. Attention was called to the various difficulties encountered and for this reason a simpler and surer method was desired.

The method described has fulfilled all the desired requirements and has been used in many transfusions with excellent results.

The donor set consists of a No. 13 gauge, 2½ inch needle with a sharp short bevel,[1] a 1000 c.c. flask and a piece of glass tubing 8 inches long with a diameter of 4.5 mm. to 4.6 mm.

One end of the glass tubing is ground down on a fine emory wheel to fit the adaptor of the needle. The tubing is then bent at right angles in a Bunsen burner flame, in the directions shown in Figure 1. Although it is not essential, better results are obtained if the glass tube is coated with an ether-paraffin solution made with 2 drams autoclaved paraffin mixed with two ounces of ether, before using.

TECHNIQUE

After the usual skin preparation, the skin over and around the vein is injected with 1 per cent novocaine solution. A tourniquet is applied above the site of injection and the needle is inserted into the vein, directing the point proximally, in the direction of the hand. As the vein is entered by the needle there is usually a gush of blood from the needle which can be controlled by a gloved finger until the glass tubing can be inserted into the needle. The blood then runs freely from the tube and is caught in a flask containing the sodium citrate solution. (Fig. 1-2.) A constant stream of blood is maintained by the donor slowly opening and closing his hand. It is rarely necessary to dissect a vein with this technique. When this is indicated, as when the donor is obese or has small veins, this method works just as efficiently.

With this method the vein is usually saved for future use, if needed. The whole procedure is painless, except the initial prick of the needle injecting novocaine and there is no residual tenderness in the arm.

I wish to thank Mr. J. F. Glore of the Illustration Department for these illustrations.

[1] Made by Becton, Dickinson & Co. Rutherford, N. J.

* From the Department of Surgery, University of Indiana Medical Center.

[From Fernelius' Universa Medicina, Geneva, 1679.]

BOOKSHELF BROWSING

AN INQUIRY INTO SEVERAL BELIEFS HELD BY MAN REGARDING THE ANATOMICAL SITE OF THE SOUL*

WILLIAM M. MILLAR, M.D.

CINCINNATI, OHIO

" . . . AMONG knowable things, nothing is alike noble, as is the knowing of the Soul itself. . . . "—VAN HELMONT.

INTRODUCTION

Since the beginning of Time apparently man has busied himself with the enchanting, fascinating but still unsolved question, "Where and what is the soul?" There have been individuals who have doubted its being, arguing that it did not exist; others have held that because there *is* life, a soul, whatever it may be, must be present also. Ignorance has not prevented the writing of an almost countless number of tomes regarding the exact nature of the soul, and in all ages there have been religious factions and cliques which held stoutly to this creed or to that opinion. It is possible here to mention but a few of these many theories.

Soul Sleep or Psychopannychism. This idea apparently originated with the Armenian and Arabian sects and, although it was condemned by the various Christian Councils of the Middle Ages, Pope John XXII accepted it openly. At the time of the Reformation it was revived by several factions and was even extensively developed by the Anabaptists. One of its chief theological opponents, by the way, was the dour Swiss, John Calvin, the "father" of Presbyterianism.

Soul-death or Thnetopsychism, is another development of this "motif" and it was believed, for example, by one Petrus Pomponatus (circa 1500 A.D.) that the soul was actually "dead" from the death of the body to the moment of the beginning of the "Last Judgment."

Transmigration of Souls. It is well known that this is a common belief of many peoples and races.

Soul Sex. Some philosophers affirm that the various viscera have their own separate male soul. The Sages of China have elaborated upon this dogma and some of them have maintained that every human being is provided with both a male and a female variety, and explained this physical hermaphroditism by the "need" of a harmonious cooperation of these two into one organic unity!

* From the Department of Surgery of the College of Medicine of the University of Cincinnati and of the Cincinnati General Hospital.

Traducianism, the theory of the derivation of the child's soul from that of his parents; Creationism, that every soul born into the world is a fresh creation, Phyletic Psychogenisism, the tissue soul of Haeckel, are only a few more mellifluorous labels that have been plastered onto this problem. Dozens of others might be discussed but it is not the purpose of this brochure to review such polemic discussions, for it is concerned only with the alleged *place* or the "anatomical abode" of the soul. As we have said, the topic has ever been a great subject of discussion though candidly there is perhaps no better or more applicable statement than that taken from Lucretius, "None knows the nature of the soul, whether it be born with us, or infused into us at our birth, whether it dies with us, or descends to the shades below, or whether the gods transmit it into other animals." (De Rerum Natura 1: 112.)

However, in extenuation and in partial justification, at least, for this monograph we quote from the Oriatrike of van Helmont: "He that shall first draw forth the essayes of the Soul and afterward drink down the juices of Nature, in his Return . . . shall be of a larger capacity than he was in his former reading. . . . "

Assyrian. Jastrow has given us an excellent description on the importance of the liver in the religion of antiquity. With the Assyrians this organ was the site of the lower emotions such as envy, jealousy, and ill humor. They also argued that since life of all kinds was due to the gods a part of some one object in man acted as a representative of the deities, and was therefore the site of the soul. Or to phrase it another way, a certain portion of the body was really the mirror in which the gods' minds and actions were reflected and to these dwellers by the Euphrates the liver seemed to be such a center of vitality. Hepatoscopy was done to such an extent that in Assyria sheep livers were used for divination as early as 3000 B.C., and special attention was then paid to the importance of the various lobes, the gall bladder and the portal vein. Indeed, the Babylonian priests prepared clay models to be used by their young theological students and specimens may be found today in almost any museum of Oriental lore.

Egyptian. The Egyptians considered that after death their soul assumed the shape of a bird which in the early years of the country's existence was a heron but in later dynasties became a human faced avian. But besides this soul, man also possessed a kind of guardian angel called Ka, which was incarnated into one or more material objects in the tomb and which represented a "material" support which "lingered" long after the mummy had disappeared. The soul of a dead man always appeared before Osiris to be weighed and forty-two judges sat in council, each individual being compelled to answer a great number of questions. After proper and unbiased judgment the good became "Osiresses" and thereby identified themselves with the royal deity. The bad were packed off into Hell.

Greek. Plato's (431 B.C.–351 B.C.) essay "Timaeus," well known and often quoted, divides the soul-matter into an upper and a lower kind. The lower soul is endowed with "courage and spirit . . . they settled in the interval between midriff and neck . . . and as the heart was liable to become heated . . . lung was implanted to help as a buffer and to act as a cooling agent. . . . The part of the soul which desires meats and drinks they placed between midriff and the navel (in) the liver, the immortal part or reason in the head."

In "Phaedrus" is the famous comparison of the dual soul of man with a pair of winged chariot horses in harness. The human charioteer drives one of noble breed and one of ignoble, and his chief aim of life is to keep the two under control.

Aristotle (B.C. 384–322). Those who know Aristotle will immediately recall his "De Anima" in connection with this subject where the various theories held by prominent men and philosophers up to that time are stated and described. In this

magnificent work is mentioned how Heraclitus identified the soul with vapor from which he derived all other principles and thought it to be in a ceaseless flux, and stated that it is the least corporeal of things. Hippon asserted that the soul was water and based his statement on the fact that the seed of all animals is moist. He continues to argue that the blood could not be the soul because semen is not bloody. In direct opposition to this view, others, among whom was Critias, maintained that the blood held the soul. Diogenes associated the soul with air and thought the latter was composed of the minutest of particles and was the "first principle." Democritus and Anaxagoras treated the mind as a single nature.

Practically all philosophers, according to Aristotle, defined the soul from the three characteristics of motion, perception and incorporeality. Some held to one single element, while others were convinced equally of plurality. Aristotle himself did not believe the soul was capable of motion, although Thales considered it as the cause of motion and affirmed the lodestone to possess a soul because of its property to attract certain objects.

Empedocles, who antedated Plato and Aristotle by two hundred years, is quoted by almost all writers on this subject. He was firmly convinced that the blood was the soul.

In the blood streams, back leaping into it,
The heart is nourished, where prevails the power
That men call thought; for to the blood that stirs
About the heart is man's controlling thought.
(Leonard's translation of paragraph 105.)

From Epicurus, the Greek philosopher who lived some three hundred years before Christ, we read:

(63.) . . . You must consider that the soul is a body of fine particles distributed throughout the whole structure, and most resembling wind with a certain admixture of heat, and in some respects like to one of these and in some to the other.

(64.) . . . The Soul possesses the chief cause of sensation, yet it could not have acquired sensation, unless it were in some way enclosed by the rest of the structure. And this in its turn having afforded the soul this cause of sensation acquires itself too a share in this contingent capacity from the soul. Yet it does not acquire all the capacities which the soul possesses; and therefore when the soul is released from the body the body no longer has sensation. For it never possessed this power in itself, but used to afford opportunity for it to another existence, brought into being at the same time with itself. . . .

(65.) . . . Therefore, so long as the soul remains in the body, even though some other part of the body be lost, it will never lose sensation; nay more, whatever portions of the soul may perish too, when that which enclosed is removed either in whole or in part, if the soul continues to exist at all, it will retain sensation. On the other hand the rest of the structure, though it continues to exist either as a whole or in part, does not retain sensations if it has once lost that sum of atoms, however small it be, which goes together to produce the nature of the soul. Moreover, if the whole structure is dissolved, the soul is dispersed and no longer has the same powers nor performs its movement so that it does not possess sensation either. . . .

Epicurus continues and goes on to say that the soul cannot be incorporeal for if it were like the only incorporeal independent existence, the void, it could not act or be acted upon in any way.

Plutarch (A.D. 46–120) in his "Morals" reviews the question of a soul with considerable thoroughness. He declares that Asclepiades, the famous physician, believed that the soul was concurrent with the excitation of the senses. He mentions that Heirophilus put it in the sinus which is at the base of the brain, that Paramenides placed it in the whole breast, Erasistratus in the membrane involving the brain, while the Stoic philosophers thought it equivalent with hot breath. According to the historian this last school said that the soul was composed of eight composite points; five of these are the senses, hearing, seeing, touch, taste and

smell and the other three are speaking, generation and thinking. After locating the soul in the human organism he becomes concerned with the soul of the world itself and cites Heraclitus who thought it to be the "exhalations" (clouds? mist?) which procede from the most part of it.

Roman. Lucretius (B.C. 96–55), that magnificent intellect of the Roman Golden Age who knew something of everything from astronomy to gynecology, who described the atomic theory and even the Weismannian biologic theorems in his beautiful poem "De Rerum Natura," gives us this idea of his conception of the Soul:

Accordingly the whole spirit must consist
of very small seeds being interlaced through veins,
flesh and sinews; wherefore, when the whole has already
departed from the body, nevertheless the outward contour
of the limbs presents itself undiminished, nor is one jot
of the weight lacking . . . (iii, 216 et seq.)

It seemed to this distinguished Latin that the soul was a composite structure for it was composed of breath, heat, air and a fourth nameless substance, a kind of spirit of the spirit, one might say. The mind and the body do not correspond atom for atom as the former are fewer, smaller and even less in number, and when a man dies "piece-meal," as from a gangrenous leg, the soul also dies a kind of a lingering death since it is not confined in any one particular place. Furthermore, this philosopher thought that the spirit is not immortal since an individual can not remember his former existence and he refutes the concept of the transmigration of souls because the person concerned would then show mixed characteristics. The soul may also be subject to disease and death.* Since we felt nothing before our birth we shall feel nothing after our demise.

* This idea would make Lucretius one of the world's earliest psychiatrists.

Marcus Tullius Cicero, in his "Tusculan Disputations" (45 B.C.), gives a birdseye view of the various beliefs held by his predecessors and after admitting and acknowledging his debt to Plato naively says, "Further, as to what the soul is in itself, or where its place is in us, or what its origin, there is much disagreement."

Hebrew. The Bible.* To express the location of the human soul the Hebrews in the Old Testament used at least three expressions for they seem to locate it in the blood, the heart and the intestines. These expressions are somewhat wide in their use.

1. In the *blood.* (Other passages could be cited if space permitted.)

In forbidding the eating of blood, these statements are used:

Leviticus 17: 10, 11 "And whatsoever man there be of the house of Israel, or of the strangers that sojourn among you, that eateth any manner of blood; I will even set my face against that soul that eateth blood, and will cut him off from among his people. *For the life of the flesh* (is) *in the blood.*"

Genesis 9: 4. "But flesh with *the life thereof,* (which is) *the blood thereof,* shall ye not eat."

Deuteronomy 12: 23. "Only be sure that thou eat not the blood: *for the blood* (is) *the life:* and thou mayest not eat the life with the flesh."

2. In the *heart.* As the heart is in the center of the blood, the heart is represented as the seat of life, thought, will, the acting principle.

Note in the following texts:

Exodus 35: 22. "And they came, both man and women, as many as were *willing-hearted* (literally, *willing of heart*), and brought bracelets, and earrings, and rings and tablets, all jewels of gold: and every man that offered an offering of gold unto the LORD."

1 Samuel 14: 7. "And his armourbearer said unto him, Do all that (is) *in thine heart:* turn thee: behold, I (am) with thee according *to thy heart.*"

* The author wishes to acknowledge his debt to his father, Dr. Charles C. Millar, for the references used in this particular section. They were taken directly from the Hebrew text.

Speaking of the Assyrian, it is said, in Isaiah 10: 7. "Neither *doth his heart think* so."

3. In the *intestines*, though this may be for *inward parts* in a more general sense.

1 Kings 17: 21, 22. "And he stretched himself upon the child three times, and cried unto the LORD, and said, O LORD my God, I pray thee let this child's *soul come into him again*. (literally, *into his inward part*.) And the LORD heard the voice of Elijah; and the *soul* of the child *came into him again*. (Literally, into his inward part) and he revived."

Psalm 5: 9. "Their *inward part* is very wickedness."

Genesis 41: 21. "And when they had eaten them up, (Literally, they had gone into the *inward parts* of them), it could not be known that they had eaten them. (Literally, that they had gone into the *inward parts* of them.)

Exodus 29: 13. "And thou shalt take all the fat that covereth *the inwards* . . . and burn (them) upon the altar."

Psalm 49: 11. "Their *inward thought*." (literally, "their *inward part*.") "Their inward thought (is), that their houses (shall continue) for ever, (and) their dwelling places to all generations; they call (their) lands after their own names."

Talmud. In addition to the opinions expressed in the Old Testament there are, of course, other views set forth by the Jews and in the Talmud there is no more interesting story than that incident to the bone Luz. There are at least two accounts of this marvelous vertebra, in "Der Midrasch Kohelet" and "Der Midrasch Wajikra Rabba," which furnish interesting and amusing reading. The word itself is derived from the Aramaic and means "almond." In these two references is an account of an alleged conversation between one, Joshua, the son of Chanin, and the Roman Emperor Hadrian (Circa 130 A.D.). The latter, so runs the narrative, once asked the Jew how God would resurrect man in the world which was to come. The reply was that it would be through LUZ, a bone in the spinal column. When asked how he knew this and how such a striking assertion could be proved, the Rabbi is said to have produced the bone! This could not be destroyed with fire, nor was it soluble in water. Not even when placed on a blacksmith's anvil and lustily beaten with a sledge was there any sign of destruction and indeed the forge split after a few ringing strokes, leaving Luz absolutely uninjured. We might remark in passing that Joshua was a tailor and not an anatomist by profession.

Neo-christian. Tertullian, a prolific, belligerent and positive writer, who lived in the second century after Christ's birth and who wrote among many other things a "Treatise on the Soul," reviews the subject and cites the opinion of various "pagan" philosophers. Among those who have not been mentioned elsewhere in this paper are: Moschion, who declared that the soul floats about through the whole body; Zenophenes, who placed it in the crown of the head; Herophilus, who located it at the base of the brain (vide Plutarch); Strato who located it in the membranes of the brain; and another Strato, the physician, who placed it between the eyebrows.

Tertullian continues the discussion and says it was quite an easy question to decide and without any difficulty placed it in the heart, and for proof he nimbly quoted from the Bible to this effect: "Create in me a clean heart, oh, Lord." (Psalms LI: 10.)

The anti-Nicene father, Lactantius, "On the Workmanship of God," quotes Varro, "The soul is air conceived in the mouth, warmed in the lungs, heated in the heart, diffused through the body."

Buddhism. Buddhism does not hold to the belief of a soul and indeed "anattam," the absence of self, is an abiding principle of the three parts of wisdom and perception. But diametrically opposite to this dogma stand the Gainas, one of its quite powerful sects, a subdivision said to have been founded by Mahavira who believed and taught that there were numerous souls embodied in animals, gods, plants, hell-beings and even in the four elements water, earth, wind and fire.

Brahmanism. Anyone who is in any way familiar with the Brahmanic religious literature will recall the hundreds of pages written on the various ideas of "self." In the main they are as hard to peruse as the philosophy of Emanuel Kant!

While in one place of the Vedanta-Sutras it is stated that, "It is nowhere the purpose of Scripture to make statements regarding the individual soul" (I Adhyâya 3, Pâda 7) and elsewhere (II Adhyâya 2, Pâda 17) we read that conjunction cannot take place between the atoms, the soul and the internal organs because they have no parts. In other portions there exist several citations which would place the soul in the heart (I Adhyâya 3, Pâda 14). The soul is called a part of Brahman, a metaphor as one commentator with child-like candor carefully indicates. Ideas on "Self" and the soul as "pure intelligence" and "non-active infinite" are discussed. There is a connection between the "intelligent self" and "vital air" which sustains the body and the individual soul as well as the "chief vital air" may be justly designated as the "Intelligent Self."

In Adhyâya 3, Pâda 19, the soul is stated to be of atomic size because of its ability to pass in and out of the body. To quote Paragraph 20,

> Either from the eye or from the skull or from the other places of the body (the Self passes out). . . . He taking with him those elements of light descends into the heart. Paragraph 23. Just as a drop of sandal ointment although in contact with one spot of the body only, yet produces a refreshing sensation extending over the whole body: so the soul, although abiding in one point of the body only, may be the cause of a perception extending over the entire body. And as the soul is connected with the skin (which is the seat of feeling) the assumption that the soul's sensation should extend over the whole body is by no means contrary to reason. For the connexion of the soul and the skin abides in the entire skin, and the skin extends over the whole body. . . .

A reason which is used against this argument is the remark that the soul abides in the heart. But though the soul *is* in the heart, by means of passages up to the hairs and up to the tip of the nails it is able to pervade the entire body by means of "intelligence."

In the "Bhagavadgîtâ" (Chap. v, 19) we learn that the self-restrained embodied (self) "lies at ease" within the city of nine portals (i.e., the eyes, nostrils, ears, mouth and two excretory orifices. Elsewhere in dealing with sacrifices it is stated:

> For the heart is the self (soul), the mind; and the clotted ghee is the breath. (Satapatha—Brâhmana, III Kânda, 8 Adhyâya 3, Brahmana 10; 8.)

In the Anugitâ (Chap. III, 7): "That soul entering all the limbs of the foetus, part by part, and dwelling in the seat of the life-wind, supports (them) with the mind. Then the foetus becoming possessed of consciousness moves about its limbs. . . . "

(Chap. II, 34) "The soul being without a fixed seat is shaken about by the wind . . . (the wind here being something exuding from a vitally wounded part).

Comparison is made here with those individuals who have eyes of knowledge which are able to see a soul departing from the body or entering the womb with those who have eyes that are able to see a glow-worm disappear here and there in the darkness. This paragraph recalls to twentieth century minds the "ectoplasm" experiments that have been conducted during the past few years.

Orphic Beliefs. Aristotle states that the Orphic poems maintain that the soul "is from the universe in the process of respiration being borne upon the winds."

Mohammedan. According to Hughes, the Mohammedan writers hold very conflicting views concerning the state of the soul after death. All agree that the Angel of Death, Malaku 'l-Maut, separates the human soul from the body at the time of death and performs this act with ease and kindess to the good and with "force and violence" towards the wicked. This idea is based on the verse in the Qur'ân Surah (XXIX) where the Prophet swears by those

"who tear out violently and those who are gently released." Apparently there is no one fixed central portion which is the abode of the soul. However, we know that the spirits of the faithful are divided into several classes. There are those who, at death, are admitted immediately into Paradise and the spirits of martyrs who rest in the crops of green birds which eat the fruits and drink of the waters of Paradise. Then there are those spirits of all the remaining believers who either remain near the grave for several days or until the time of the Resurrection or who may, indeed, be placed in the lowest heaven with Adam. The Prophet states that he saw them there during his trip to Heaven; and finally those departed spirits who live in the form and assume the shape of white birds and roost and perch under the throne of God. The bad go down into Hell, or Sijjin, where they are tortured and interminably tormented.

The soul itself appears to have a guardian for in the Chapter of the Evening Star one reads: "Verily every soul has a guardian over it." In still another portion of the Qur'ân blessing is promised: "Prosperous is he who purifies it (i.e., the soul)."*

The philosopher and surgeon, Avicenna, a Persian Mohammedan of note (980–1037 A.D.) in his "Compendium of the Soul" arranges spiritual faculties in three groups: plant or vegetable power, animal power, and the speaking or rational power. The Persian joins the five senses of taste, touch, smell, seeing and hearing with the five inward senses, i.e., common sense, the imaginative, "vis cogitative," memory and the "vis existimative."

In Section Nine in "Which Proofs of the Essentiality of the Soul and of Its Independence of Body in its Structure are Set forth in pursuance of the Method of Logicians" the conception is that the soul is not a corporeal, organic power. Proof is adduced that if it were it would be within some organ of man which would "wither" when the organ itself started to disintegrate. This medical man would establish a "mental essence" quite distinct from bodies but which would stand towards the human soul in the way that light does with regard to sight. In passing it may be noted that the "sway" of the picturing representing common sense is located in the anterior "hollow" or ventricle of the brain; the control of the imaginative in the middle "hollow"; conjecturing through the entire brain. The "compartment" of the imagination is placed within the brain, and "in so far as these hollows suffer harm and hurt, so will the manifold working of these powers suffer also. . . . "

* From the Chapter of the Sun of the Qur'ân, verse 9.

SOME EUROPEAN VIEWS DURING THE SIXTEENTH AND SEVENTEENTH CENTURY

Montaigne, (1533–1592), the scholarly Frenchman in his "honest book" of Essays, gives an excellent, concise sketch of the various beliefs held by the ancients. Among those not mentioned elsewhere in this monograph are Posidonius, Cleanthes, and Galien who thought the soul was the body heat or "hot complexion"; Hippocrates and Herophilus who antedated Avicenna in placing it in the ventricles of the brain (vide Plutarch), Epicurus in the stomach, the Stoics "about or within the heart," and Chrysippus who also "argued it to be about the heart."

Like Cicero, from whom this able essayist draws freely, the Bordeaux scholar has succeeded in summarizing a tremendous number of citations in a few paragraphs but adds no startling original conceptions of his own.

Van Helmont. In Europe during the sixteenth century were many erratically erudite individuals, one of the most prominent being Jean Baptiste van Helmont. Born in the Low Lands in 1577, he was educated at the Louvain and after much travel settled down to matrimony and a scientific career in a suburb of Brussels. Best recalled to the modern age for his work in pneumatic chemistry (he was the first man to use the word "gas"), this independent thinker refused to consider

fire and earth as elements and to his own mind's satisfaction successfully reduced matter to air and water. But in order to explain properly the mechanism of life this talented individual was forced to manufacture an elaborate and complicated system. Briefly there was a central *archeus* which controlled a number of lesser *archei*. Diseases were due to an injury of this *archeus*. In addition there was a "sensitive soul" which was the "husk" or covering of man's immortal soul. Why? Because a severe blow here would cause unconsciousness! To quote from his *Oriatrike* or *Physic Refined:**

In Chapter XLII the worthy doctor holds to the argument that the stomach and the spleen run the body. "For of the Spleen and the Stomach I make only one Wedlock and one Marriage-bed. . . . "

Chapter XXXVII: For it was never the study or the office of the soul to wander or pass from place to place, that it may chase out a Bride-bed for itself . . . In the stomach is placed the desirable Inn of the Soul . . . (18). Therefore the radical Bride-bed of the Sensitive Soul is the vital Archeus of the stomach, and it stands and remains there for the whole life time not indeed, that the sensitive soul is entertained in the stomach, as it were in a Sack, Skin, Membrane, Pot, Prison, little Cell, or bark; neither is it comprehended in that feat in manner of Bodies enclosed within a purse, but after an irregular manner it is centrally in a point, and as it were in the very individual middle of one membranous thickness. And it is in a place nevertheless, not plainly locally. . . .

Stahl (1660–1734) and de Sauvage (1706–1767) were later proponents and elaborators of von Helmont's grandiose conceptions.

Descartes, one time soldier, physiologist, and always the eternal philosopher, believes the soul is essentially "thinking," the body is an "extended substance," and the two are "desperate realities." He argues accordingly that there must be a place where these two can be coordinated and selects the pineal gland for the following reasons:

In the chapter "The Passions of the Soul" is Article XXXI which is entitled "That there is a small gland in the brain in which the soul exercises its function more particularly than in the other parts." We read,

It is necessary to know that although the soul is joined to the whole body, there is yet in that a certain part in which it exercises its functions more particularly than in all the others, and it is usually believed that this part is the brain, or possibly the heart; the brain because it is with it that the organs of sense are connected and the heart because it is apparently in it that we experience the passions. But, in examining the matter with care, it seems as though I clearly ascertain that the part of the body in which the soul exercises its function immediately is in no wise the heart, nor the whole of the brain, but merely the most inward of all its parts, to wit, a certain very small gland which is situated in the middle of its substance and so suspended above the duct whereby the animal spirits in its anterior cavities have communication with the posterior; that the slightest movements which take place in it may alter very greatly the course of these spirits, and reciprocally that the smallest changes which occur in the course of the spirits may do much to change the movements of this gland. . . .

Article XXXII, "How do we know that this gland is the main seat of the soul?" Here the Frenchman reasons that as there are two images from our two eyes there must be some spot where the "impressions can unite before arriving at the soul in order that they may not represent to it two objects instead of one." . . . He continues, "It is easy to apprehend how these images or impressions might unite in this gland by the intermission of the spirits which fill the cavities of the brain; but there is no other place in the body where they can thus be united unless they are so in this gland." Article XLXI is on "Memory" and here it is stated that the pineal

* The copy from which this account has been taken was published in 1662 and has been "faithfully rendered into English in tendency to a common good and increase of true science by J(ohn) C(handler) sometime M. H. of Oxon."

body rotates, thrusting and shunting the spirits off to the various parts of the brain!

Space will not permit elaboration of the idea of many other no less famous individuals who wrote on the subject, only a few being briefly mentioned. In passing it may be said that these gentlemen, together with practically everyone of their time, believed that the site of the soul and the seat of life were identical. With this in mind the modern reader can view their physiological and metaphysical struggles with much more sympathy and understanding.

Thomas Willis (1622–1675), the famous English anatomist, placed his "anima rationalis" in the cerebrum and the "anima vegetiva" in the cerebellum. He based his reasons on the fact that death followed when the vagi nerves were cut.

Tulp, the illustrious Dutchman, the "original" surgeon in Rembrandt's painting, also placed it in the cerebellum.

La Peyronie (1679–1748), better recalled today for his "disease," was one of the first who took issue with Descartes's idea that the pineal body was the seat of the soul as he declared that he had seen wounds of this organ in which immediate death had not ensued. About the same period others,* however, disagreed with the two Frenchmen because they argued that the pineal was larger in animals than in man, and as their souls were certainly no bigger, better or larger, it could be immediately seen that this spot certainly was not the exact location. La Peyronie wanted to put it in the corpus callosum and in this opinion he was later abetted by Chopart (1743–1795). Of course there was disagreement to this as Vieussens (1641–1715) had placed the soul in the "white brain"; Boerhaave (1668–1738) in the gyrus fornicatus; Mayow (1643–1679), Pacchioni (1665–1726) and Santorini (1681–1737) in the dura mater. Mayow, moreover, succeeded in making the situation more complicated than ever for he introduced the chemical factor into the already perplexing question for the first time.

Opposed to these concepts was Meig (b. 1741) for he put the human soul in the spinal cord because he had seen several acephalic babies who had lived for a short time after birth. He reasoned that since these monstrosities had been born they must certainly have souls, and as they had lived without heads the soul could not be located in this nerve organ. Therefore, the "place" must be located in the only large remaining portion, the spinal cord!

La Mettrie (1709–1753), the founder of materialism in France, Haller, the Swiss physiologist (1708–1777), and Marat, the mad doctor of the French Revolution, are a few of the many men of the eighteenth century who found time to become interested in the question.

All of these studies were serious, but of course there had to be ribald wits and amusing satirists who viewed the problem with a sardonic and with more amusing and refreshing views. Chief of these was Alexander Pope. This Englishman aided by Arbuthnot, the originator of John Bull, in "Martinus Scriblerus" gives us a look which is far from the pedantic and scholastic ideas we have so far reviewed. A few portions of this work are well worth quoting:

Martinus Scriblerus

(Chap. xii)

How Martinus Endeavoured to Find Out the Seat of the Soul, and of His Correspondence with the Free-Thinkers.

In this Design of Martin to investigate the Diseases of the Mind, he thought nothing so necessary as an Enquiry after the Seat of the Soul; in which at first he laboured under great uncertainties. Sometimes he was of opinion that it lodged in the Brain, sometimes in the Stomach, and sometimes in the Heart. Afterwards he thought it absurd to confine that sovereign Lady to one apartment, which made him infer that she shifted it according to the several functions of life: "The Brain was her

*The interested reader is referred to Révész's excellent work on the Soul in which this portion has been treated in great detail.

Study, the Heart her State-room, and the Stomach her Kitchen." But as he saw several Offices of life went on at the same time, he was forced to give up this Hypothesis also. He now conjectured it was more for the dignity of the Soul to perform several operations by her little Ministers, the Animal Spirits, from whence it was natural to conclude, that she resides in different parts according to different Inclinations, Sexes, Ages, and Professions. Thus in Epicures he seated her in the mouth of the Stomach, Philosophers have her in the Brain, Soldiers in their Heart, Women in their Tongues, Fiddlers in their Fingers, and Rope-dancers in their Toes. At length he grew fond of the Glandula Pinealis, dissecting many subjects to find out the different Figure of this Gland, from whence he might discover the cause of the different Tempers of mankind. He supposed that in factious and restless-spirited people he should find it sharp and pointed, allowing no room for the Soul to repose herself; that in quiet Tempers it was flat, smooth, and soft, affording to the Soul as it were an easy cushion. He was confirmed in this by observing that Calves and Philosophers, Tigers and Statesmen, Foxes and Sharpers, Peacocks and Fops, Cock-Sparrows and Coquets, Monkeys and Players, Courtiers and Spaniels, Moles and Misers, exactly resemble one another in the conformation of the Pineal Gland. He did not doubt likewise to find the same resemblance in Highwaymen and Conquerors: In order to satisfy himself in which, it was, that he purchased the body of one of the first Species (as hath been before related) by Tyburn, hoping in time to have the happiness of one of the latter too, under his Anatomical knife. . . .

And as where there is but one Member of Generation, there is but one Body, so there can be but one Soul; because the said Organ of Generation is the seat of the Soul; and consequently where there is but one such Organ, there can be but one Soul. Let me hear say, without injury to truth, that no Philosopher, either of the past or present age, hath taken more pains to discover where the Soul keeps her residence, than the Plaintiff, the learned Martinus Scriblerus; and after his most diligent enquiries and experiments, he hath been very persuaded, that the Organ of Generation is the true and only Seat of the Soul. That this part is seated in the middle, and near the centre of the whole Body, is obvious. From thence, like the sun in the centre of the world, the Soul dispenses her warmth and vital influence. Let the brain glory in the Wisdom of the aged, the Science of the learned, the Policy of the statesman, and the Invention of the witty; the accidental Amusements and Emanations of the Soul, and mortal as the Possessors of them! It is to the Organs of Generation that we owe Man himself; there the Soul is employed in works suitable to the dignity of her nature, and (as we may say) sits brooding over ages yet unborn. . . .

Primitive Races. A great mass of data has been collected by anthropologists during the last few years regarding the views of the primitive tribes throughout the world. The contributions of Hastings and Frazier have been particularly valuable along these lines and it is from their books that most of the following information has been gathered.

Multiplicity of Souls. The Dyaks of Malaysia and Borneo believe that every man possessed seven souls, the Alpoors in the Celebes and the Battas believe that he has but three. The Abougmes in Laos maintain that fully thirty spirits reign in the hands, the eyes, the lips and the other parts of the body. In the Occident the West Indian Carib thought that there was one soul for the heart, another for the head and that one even existed in a pulsating artery. Washington Mathews in his account of the Hidatsa Indians in Northwest America, declared that this tribe explained gradual death by presupposing that man possessed four souls and that after death these slipped consecutively from the body. Demise was complete only when all had left the corpse.

According to Groot, certain ancient Chinese philosophers attributed two souls to man, the "shen" or immortal, the "kiver" or material portion which will stay in the grave of the buried man. Other oriental sages believed in a multiplicity of souls, the number depending on the individual, his age and the condition of the character of his various organs. The heart was considered the seat of vital spirits, to

others the five viscera of the body acted as "depots" for various attributes; the lungs "billeted" righteousness, the liver, benevolence, the kidneys, knowledge, the heart, ceremony, and the spleen, trustworthiness. Dreams are the peregrinations of the soul.

The Soul of the Afterbirth. The Australian aborigines of Queensland and the Battas of Sumatra considered the umbilical cord and the placenta as a living external soul.* The ancient Islander declared that a child's guardian spirit, or part of his soul, had its site in the chorion, called by them the "fylgia," and that this part of the afterbirth should never be thrown away lest the demons get it. Neither should it be burned for the newborn baby would then have no spirit. The parents were accustomed to bury it under the doorway and over this spot the mother would step. In this way it could be guarded and watched. Furthermore, if the chorion was created in the afterlife its guardian spirit would or could assume the figure of a bear, a wolf, or some such animal.

Hair. A tribe in one of the Dutch East Indies on an island west of Sumatra, have a curious legend. In their folklore stories they tell of a chief who once upon a time was captured by his enemies. His captors tried repeatedly to kill the unfortunate man but without success for everything, even fire and water, would not destroy him. At last they prevailed upon his wife to reveal the secret of the captive's charmed life and Delilah-like she did. It seemed that on her husband's head was a hair which was as hard as copper wire, and it was in this and with this that his life was bound. At once this was plucked by his foes, and immediately the poor victim expired!

Intestines. The Khasis of Assam have a variation of this story: There was once a King named Kyllong of Mada who was so strong that no one could "permanently" kill him. However, his rival managed to capture him and would repeatedly chip him to bits, but the next day always found the sturdy individual completely reconstructed and very much alive. This continued for some time until finally the chief was "framed" by a beautiful slave wife who was given to him and who continually coaxed him to tell her his secret. He refused to do this for some time for he undoubtedly suspected a ruse but finally the poor man succumbed to her pleadings. The monarch informed his beautiful mate that he was compelled to bathe every day and at the same time to "wash his entrails." After this self administered enema he could and would only take food, and no one could overcome him unless they "secured" his intestines. Of course, as soon as his mistress obtained this information she informed her true friends and the poor king's gastrointestinal tract was soon cut to pieces in short order. Then and then only did his soul leave him and he ceased to live.

Spinal Cord. The natives of New Zealand believed that the soul was located in the spinal "marrow" (Goome).

Modern Beliefs. Time will not permit an elaboration of the European and American views of the nineteenth and twentieth centuries of the Christian Era. The reader is referred to Norman Pearson, Ernest Haeckel, Vogt, and others for detailed discussions on the subject. Briefly, the attempt has been made to restore the soul to a function of the cell, although there are those who deny (Edison) that there is any soul whatsoever. Haeckel would have it that every living cell has its own psychic properties and that a "tissue-soul" develops with progressive cellular changes. Stahl and Hudson presupposed the soul to be diffused throughout the entire body while Lotze theorized that it was only in contact with the brain at highly differentiated parts. There are numerous other philosophers who believe that as the body is evolved the soul has progressed hand in hand, so to speak, with it and would not confine it to any mono-

* The early Christian Church here encountered technical difficulties and there was at least one church council that tried to settle the baffling problem as to whether or not human afterbirth was immortal.

cellular activities. From the physiochemical aspect we find in the last decade one man, Mathews, who ascribed a soul to the atom which may enter and leave hydrogen. We quote, "(A soul) is a minute portion of luminiferous ether, of time and space, of eternity and infinity."

In concluding there is perhaps no more fitting quotation with which the entire subject regarding the site of the human soul may be summarized than the following taken from "The Religio Medici" of Sir Thomas Browne: "In our study of Anatomy there is a mass of mysterious Philosophy and as such reduce the very Heathens to Divinity yet amongst all those rare discoveries and curious pieces I find in the Fabrick of man . . . no Organ or Instrument for the rational Soul. . . . "

REFERENCES

Aristotle. *De Anima. See also the Introduction of De Anima* by R. D. Hicks. Cambridge University Press, 1907.

Avicenna. Compendium of the Soul.

Bible. See references cited in text.

Bibliotheca Rabbinica (Midrasch Kohelet). Leipzig, *Ib* Otto Schulze, 1880, cap. xii, V. 5, S. 153.

id. Der Midrasch Wajikra Rabba. Par. xviii, cap. xv, 1.

Brahamism. See references cited in text.

Browne, Sir Thomas. Religio Medici. Everyman Edition. New York, E. P. Dutton & Co., 1928, pp. 41–42.

Catholic Encyclopedia. New York City, Appleton Co., 1912.

Cicero. Tusculan Disputations 1, 28.

Descartes. The Philosophical Works of Descartes. Vol. 1, Articles xxxi, xxxii and xlxi. Haldane & Ross Translators, Cambridge University Press, 1911.

Empedocles, Fragments of. By William E. Leonard. Chicago, Open Court Publishing Co., 1900, 105.

Epicurus. English Translation by Bailey. Oxford Press, 1926, in section to Herodotus, Paragraph 63–65.

Frazier. Golden Bough. 3d Edition, New York, MacMillan & Co.

Garrison. The Bone Called Luz. *New York Med. Jour.*, 92: 4, 1910.

Goome. Folk Lore as a Historical Science. London, Methuen & Co., 1908.

Groot, J. J. Religious System of China. Brill, Leyden 1901, Vol. 4, pp. 5, 10, 18, 70, 114, 118.

Haeckel. The Riddle of the Universe. Translated by Joseph McCable. New York, Harper & Bro. Publisher, 1901.

Hastings. Encyclopedia of Religion and Ethics. New York City, Charles Scribner's Sons, 1908.

Hughes. Dictionary of Islam. London, W. H. Allen & Co., 1885.

Jastrow, Morris. *Transactions College of Physicians*, Phila., 29: 117, 1907.

Khasis, The. P. R. T. Gurdon; London, 1907, pp. 181–184.

Koran. See references cited in text.

Lactantius. On the workmanship of God.

Lotze. Microcosmus. Translated by Elizabeth Hamilton and E. E. Constance Jones. New York, Scribner & Welford, 1885, 1: 205.

Lucretius. De Rerum Natura, 1, 112; iii, 216 et seq.

Mathews. General Cytology. Chicago, 1924, p. 13, cited by Willy Meyer, Cancer. New York, Hoeber, 1931, p. 211.

Matthews. Hidatsa Indians. Washington, 1877, p. 50.

Montaigne. "Essays," Translated by Charles Cotton; Edited by Hazlitt. New York, A. L. Burt, Vol. 1, p. 545 et seq.

Orpheus. A General History of Religions. From the French of Salomon Reinach. By Florence Simmonds. New York City, Putnam, 1909.

Pearson. The Soul and Its Story. London, Edward Arnold, 1916.

Plato. Timaeus; Phaedrus.

Plutarch's Morals. Goodwin. Boston, Little, Brown & Co., 1871.

Pope. The Works of Alexander Pope containing principal notes of Dr. Warburton and Warton containing memoirs of Martinus Scriblerus. Vol. vi. London, J. Johnson, J. Nichols & Son, etc., 1806.

Révész, Bela. Geschichte des Seelenbegriffes und der Seelenlokalisation, Stuttgart, F. Enke, 1917.

Schaff, Herzog. A Religious Encyclopedia or Dictionary, etc. New York City, Funk & Wagnalls, 1887.

Smith and Cheetham. Dictionary of Christian Antiquities. London, John Murray, 1880.

Tertullian. Treatise on the Soul.

van Helmont. Oriatrike or Physic Refine. Faithfully rendered into English in tendency to a common good and increase of true science by J(ohn) C(handler), sometime M. H. Oxon., London, 1662.

BOOK REVIEWS

THE RELIEF OF PAIN. A HANDBOOK OF MODERN ANALGESIA. By Harold Balme, M.D., F.R.C.S. (Eng.), D.P.H. (Lond.). With an introduction by Sir E. Farquhar Buzzard, Bt. Philadelphia, P. Blakiston's Son & Co., Inc., 1936.

Sir E. Farquhar Buzzard, Regius Professor of Medicine in the University of Oxford, in the Introduction, among other things, writes, " . . . Dr. Balme, in this volume, has separated it (pain) from its familiar companions—the treatment of painless symptoms and disabilities—and, as far as possible, given it his undivided attention. He has not failed, however, to emphasize the eternal truth that the first essential in the relief of pain is a knowledge of its cause, and that the characteristics of pain often point the way to that knowledge. Nor has the author overlooked the difficulty, so well known to every practitioner of medicine, of estimating the importance of the personal or psychological factor in an attempt to assess the severity of suffering in every individual who calls for relief." In a way this is a competent book review.

Dr. Balme, in his small, well written book, divides it into four parts. Part one has the heading "The Problem of Pain" and covers The Nature of Pain, The Pathway of Pain, Sensitivity to Pain, Pain and Psychical Phenomena, The Classification of Painful Sensations, The Investigation of Pain. Part Two deals with "General and Systemic Pain (Pain from Inflammatory Disorders, from Injuries, from Disease of the Skeletal System, of the Nervous System, of the Circulatory System, and Intractable Pain)"; Part three deals with "Reginal Pain," and Part four with "The Therapeutics of Analgesia." There is a general Index.

A book that can be read with profit by all physicians.

ENDOCRINOLOGY IN MODERN PRACTICE. By William Wolf, M.D., M.S., PH.D. Illustrated. Philadelphia, W. B. Saunders Company, 1936. Price $10.00.

This work was written to provide the practitioner with a full and usable knowledge of clinical endocrinology.

The writer gives the significant features of the normal anatomy, histology, embryology, physiology and biology for each gland, so that the reader will have a background for the various endocrinopathies. The author in his preface writes, "The text has been so arranged as to provide the practitioner with a full and usable knowledge of clinical endocrinology. . . . The book has as one of its prime objects the encouragement of the physician to think along endocrine lines, no matter what his general or special field happens to be. Sections have been included on the use of gland extracts and preparations for purposes other than substitution, since this line of therapy is gaining wider and wider application. In order to aid the reader in the selection and mode of employment of endocrine substances which are commercially available, those of more or less proved merit are classified and described as to indications, composition, administration and dosage."

It has been said that the next and coming epoch in medicine will be along the lines of endocrinology. Hardly a month passes but what new facts are learned, accepted facts discarded, and these new facts may be changed a year hence. But, in this work of over a thousand pages, which includes an Index, we have the subject, in detail, up to date.

To the physician who desires the latest authoritative work on this complex subject, especially if he wishes to learn how to diagnose and treat human ailments caused by endocrine conditions, he will do well to give Dr. Wolf's book careful consideration.

THE BALANCED DIET. Logan Clendenning. New York, D. Appleton-Century Co., 1936.

This is a brief two hundred page presentation in the author's well known and popular style, of subject matter from sources rather widely apart.

A condensed review of historical contributions to the solution of the problem of man's proper diet is supplemented with a number of illustrations depicting pioneers in the field of biochemistry and nutrition. The role of the food elements and accessory factors are discussed in simple terms and the problem of the so-called deficiency diseases is emphasized. A second

division of the book discusses diet at different age periods and in various disease conditions, food fads and food economics. Tables showing food composition and caloric values are appended and a two-page bibliography cites the references to miscellaneous material from which the writer has drawn, perhaps, somewhat at random.

As an informative and entertaining collection of many bits, the book may be said to afford the reader an enjoyable literary repast, but hardly a complete and well balanced intellectual meal.

It is striking, for example, that the name of Lafayette B. Mendel, a preeminent authority on food and nutrition, is not found in the bibliography or index.

PROCTOLOGY. By Frank C. Yeomans, A.B., M.D., F.A.C.S., M.R.S.M. (London, Hon.). Price $12. Second Edition. 421 illustrations and 4 colored plates. New York, D. Appleton-Century Company, 1936.

This work has enjoyed a wide audience for the past seven years. During this time marked progress has been made in the subject. With this in mind Dr. Yeomans has revised the text and made many changes and additions. Twenty-five new illustrations have been added to this second edition.

Those familiar with the first edition will note especially the following notable changes:

Injection treatment of hemorrhoids; Oil-soluble anesthetics in pruritis ani, fissures and other rectal conditions; Radiodermatitis; Histopathy of anal crypts; Recent views on the etiology and therapy of chronic ulcerative colitis; Agranulocytic angina, anorectal involvement; Lymphopathia venera in the etiology of rectal stricture; Results of sympathetic ganglionectomy and ramisectomy in megacolon; Melanosis coli; Pectenosis and pectenotomy; Subarachnoid injection of alcohol for relief of intractible pain in advanced malignant disease; Two stage operation for carcinoma of the rectum, following the technique of Rankin and Lahey.

For the practitioner who wishes to learn about, brush up and get up-to-date on, or, at times, refer to some subject in proctology, Dr. Yeomans' book meets every need. It is delightfully written, the illustrations are a help to the text and not thrown in for padding, and the Index has been well prepared.

THE OPERATIONS OF SURGERY. By R. P. Rowlands, M.S., F.R.C.S. and Philip Turner, B.SC., M.S., F.R.C.S. Eighth Edition. Price $10. Volume 1. The Upper Extremity, The Head and Neck, The Thorax, The Lower Extremity, The Vertebral Column. 435 illustrations (38 in color). Baltimore, William Wood & Company, 1936.

This book is the direct descendant of the "Operations of Surgery," by the late W. H. A. Jacobson, first published in 1899. Recently, Rowlands, who gave so much time and work to the last three editions, died. Before his death he had done much work on the new edition, and had completed in type and manuscript about 300 pages. The remaining portion of the work was undertaken by Mr. W. H. Ogilvie, Mr. Grant Massie and Mr. A. R. Thompson. The section on Gynecology has been revised and largely rewritten by Mr. G. F. Gibberd.

There is no need to review in detail a work that is known throughout the English speaking world and is now offered in an eighth edition. Suffice to say that throughout the work stress is laid upon the indications for and against operations, and special attention is called to possible pitfalls, errors and difficulties. The editor says "We hope that this book may help readers to acquire knowledge and to avoid mistakes; but no book can possibly replace practical training and experience, which are essential for a surgeon who hopes to be worthy of his high calling." This frankness is refreshing.

This book has earned for itself a permanent place in the literature of surgery. It is a book any surgeon well might possess.

AUTHOR INDEX TO VOLUME XXXIV

Alexander, F. A. D., 428

Barach, Alvan L., 588
Barb, Jacob S., 338
Barbour, Henry G., 435
Bennett, Richard J., Jr., 374
Bickley, Robert S., 598
Bieter, Raymond N., 500
Bodley, James W., 97
Bohrer, John V., 83
Bourne, Wesley, 486
Bowen, Arthur, 122
Boyden, Allen M., 47
Branower, William, 611
Buchanan, T. Drysdale, 409
Burman, Michael S., 237

Caine, Ansel M., 463
Campbell, Meredith F., 387
Carson, William J., 379
Cheleden, John J., 581
Church, Cyril K., 41
Cogswell, H. D., 620
Cohn, Isidore, 1
Collens, William S., 71
Collins, Donald C., 107
Corff, Meyer, 241
Cullen, Stuart C., 428

Drosin, Louis, 65

Eades, Charles C., 201
Edgcomb, J. H., 57
Eiss, Stanley, 272
Emenhiser, Lee K., 104
Emmett, John L., 216

Findlay, Francis M., 395
Fiske, Frederick A., 391
Flagg, P. J., 591
Foster, George Sanford, 331, 615
Frost, Inglis F., 221

Gibson, Thomas E., 206
Glascock, Harold, 69
Glascock, Harold, Jr., 69
Glenn, Frank, 12
Golden, Benj. I., 306
Graham, Henry F., 199
Greenbaum, Frederick R., 259
Greenblatt, Robert B., 116
Guedel, Arthur E., 496

Hamilton, G. Johnson, 309
Hammer, Howard J., 119
Harris, Augustus, 125
Haskell, Benjamin, 581
Hauch, Cuyler Y., 12
Herbst, Robert H., 18
Hershey, J. H., 127
Hiller, Robert I., 352
Hobart, Marcus H., 227

Johnson, Herbert Lester, 266
Jones, Charles B., 294
Jones, R. Frank, 76

Kaufman, Justus, 365
Knoefel, Peter K., 496
Kuhn, LeRoy Philip, 254

Lahey, Frank A., 405
Lawrence, H. R., 369
Lazarus, Joseph A., 348
Lazzari, J. Henry, 316
Levy, Edward, 141
Liccione, W. T., 101
Louria, Henry W., 338
Lundy, John S., 511, 559
Lynch, Jerome M., 309

MacDonald, Ralph, 248
Maddock, Walter G., 47
Magill, I. W., 450
Malcolm, Russell L., 47
Maloney, A. H., 571
McDonnell, C. H., 90
McKechnie, Robert E., II., 286
Millar, William M., 621

Nason, Louis H., 292
Nitschke, Paul H., 94

Odom, Charles B., 547

Pankratz, David S., 104
Pettit, Roswell T., 57
Polkey, Hugh J., 18
Pollock, Leo H., 376
Pollok, L. W., 340
Pratt, Gerald H., 618
Priestley, James T., 286

Robertson, Jarratt P., 322
Robson, C. H., 468
Rosedale, R. S., 369
Rosenow, Edward C., 474
Rosenthal, Arthur A., 348
Ross, Donald E., 300
Rovenstine, E. A., 456
Ruth, Henry S., 403

Saklad, Meyer, 519
Sandler, Samuel A., 232
Schmidt, Erwin R., 408
Serafin, Peter J., 396
Sharp, Lee, 322
Singer, Harry A., 5
Sise, L. F., 419
Sword, Brian C., 539

Taylor, John A., 113
Tovell, Ralph M., 474, 531
Travers, M. P., 50
Tuohy, Edward B., 511, 544
Twinem, Francis Patton, 34

Van Werden, Benjamin de Kalb, 606
Veal, J. Ross, 606

Wagner, Lewis Clark, 357
Waters, Ralph M., 446
Wenzel, Jacob F., 119
Wilcox, Everard A., 116
Wilensky, Nathan D., 71
Willems, J. Daniel, 254
Williams, George A., 110
Wilmoth, Clifford Lee, 383
Wood, Paul M., 598
Woodbridge, P. D., 410
Wright, Arthur M., 407
Wright, Louis T., 365

Zimmerman, Leo M., 397

SUBJECT INDEX TO VOLUME XXXIV

(Bo.B.) = Bookshelf Browsing; (E.) = Editorial

Abdominal affections, acute; morphine as an aid in diagnosing, 5
Abscesses of prostate gland, 348
Absorbable tubular membrane; development and surgical applications of, 122
Allantoin, 259
A modified cecostomy, 292
Analgesia; mortality of spinal, 606
Analgesics; inhalation, in obstetrics, 463
Anesthesia and surgery (E.), 408
  a special syringe for use in spinal, 615
  carbon dioxide absorption method for inhalation, 456
  choice of, 419
  endotracheal, 450
  epidural, 547
  etiology of muscular spasms during general, 474
  evipal: its use in proctology, 581
  in children, 468
  in the medical schools (E.), 407
  intravenous, 559
  present status of inhalation, 446
  progress of, (E.), 405
  recognition of, as a specialty (E.), 409
  regional, for operations on the neck, 531
  spinal, 519
  the protective action of picrotoxin in prolonged surgical, with evipal, 571
  ventricular fibrillation in, 496
Anesthetics and liver function, 486
  surgical risk; preoperative estimation of, 410
  applied pharmacology of local, 500
  pharmacological action of inhalation, 435
  regional: agents and methods, 511
A new apparatus for artificial respiration, 611
  technique of nephroureterectomy, 206
An inquiry into several beliefs held by man regarding the anatomical site of the soul (Bo.B.), 621
Anorectal musculature, 141
  syndrome of lymphogranuloma, 316
Anuria, postoperative, 352
Apparatus, a new, for artificial respiration, 611
  inexpensive skeletal fraction, 395
  new, for reduction of fibia and fibula, 396
Appendicitis; ventral position for drainage in ruptured, 69
Appendix; argentaffin cell tumors: "carcinoids" of small intestine and, 294
  mucocele of, 383
  tuberculosis of, 379
Applied pharmacology of local anesthetics, 500
Argentaffin cell tumors: "carcinoids" of small intestine and appendix, 294
Avertin, observations on the use of tribromethanol, 598

Bladder and prostate; neurofibromatosis of, 90
  tumors; transurethral resection, 113
Block, brachial plexus, 544
  caudal and transsacral, 539
Blood transfusions; new method of indirect, 119
  simplified method of drawing blood for citrate, 620
Bones, osteosclerosis (traumatic) of carpal, 357
Bookshelf Browsing:
  An inquiry into several beliefs held by man regarding the anatomical site of the soul, 621
  Dr. Samuel A. Mudd, hero of the Dry Tortugas, 397
  Short history of stomach surgery, 127
Book Reviews:
  Cystoscopy and urography (Macalpine), 402
  Disability evaluation. Principles of treatment of compensable injuries (McBride), 139
  Endocrinology in modern practice (Wolf), 633
  Minor surgery (Christopher), 139
  Orthopaedic surgery (Mercer), 140
  Proctology (Yeomans), 634
  Short practice of surgery (Bailey and Love), 139
  Surgical diseases and injuries of the genito-urinary organs (Thomson-Walker), 402
  Textbook of histology: arranged upon an embryological basis (Bremer), 140
  The balanced diet (Clendenning), 633
  The operations of surgery (Rowlands), 634
  The relief of pain. A handbook of modern analgesia (Balme), 633
  Williams Obstetrics. A textbook for the use of students and practitioners (Stander, Ed.), 402
Brachial plexus block, 544
Breast cancer; survey of incidence in New England, 331
Burns, 254

Calculus, large vesical, 94
Cancer, breast; survey of, incidence in New England, 331
  umbilical, 116
Carbon dioxide absorption method for inhalation anesthesia, 456
"Carcinoids" of small intestine and appendix: argentaffin cell tumors, 294
Carcinoma; analysis of methods of treatment of rectal, particularly electrocoagulation, 57
Carpal bones, osteosclerosis (traumatic) of, 357
Caudal and transsacral block, 539
Cecostomy, modified, 292
Cervical infections and treatment by electrocoagulation, 221
Changing conceptions for surgical relief of prostatic obstruction, 216
Children, anesthesia in, 468
Choice of anesthesia, 419
Citrate blood transfusion; simplified method of drawing blood for, 620
Clinical and experimental study of lithotripsy, 34
Common duct, early gangrene of; perforation of gall bladder, 97
Contusion of heart with aortic regurgitation; complete recovery, 110
Critical analysis of methods of treatment of rectal carcinoma, particularly electrocoagulation, 57
Current issue of The American Journal of Surgery (E.), 403

Deformity, unusual type of Madelung-like, 365
Development and surgical applications of an absorbable tubular membrane, 122
Difficulties and dangers of injection treatment of hernia, 300
Diseases of the thyroid gland, 12
Distention; elimination of upper abdominal, by continuous aspiration during operation, 618
Diverticulosis, jejunal, 369
Diverticulum; malignant tumor of Meckel's, 101
  of ureter, 387
Dr. Samuel A. Mudd, hero of the Dry Tortugas (Bo.B.), 397

EDITORIALS:
Anesthesia and surgery, 408
Anesthesia in the medical schools, 407
Current issue of the American Journal of Surgery, 403
Fewer deaths from gall-bladder disease, 199
Present trend in surgery, 1
Progress of anesthesia, 405
Recognition of anesthesia as a specialty, 409
Electrocoagulation; cervical infections and treatment by, 221
critical analysis of methods of treatment of rectal carcinoma, particularly, 57
Elimination of upper abdominal distention by continuous aspiration during operation, 618
Empyema; treatment of acute, 50
Endotracheal anesthesia, 450
Enucleation of superior thyroid pole, 201
Epidural anesthesia, 547
Epigastric hernia, 376
Etiology of muscular spasms during general anesthesia, 474
Evipal anesthesia: its use in proctology, 581
the protective action of picrotoxin in prolonged surgical anesthesia with, 571
Examinations; observations and aids in rectal and vaginal, during labor, 65

Fewer deaths from gall-bladder disease (E.), 199
Fracture of neck of femur, gridding the femoral head and neck area in, 237

Gall-bladder disease, fewer deaths from (E.), 199
perforation of; early gangrene of common duct, 97
Gas therapy, 588
Germicide, mercresin, a new surgical, 47
Goiter; jaundice associated with toxic, 338
Granuloma venereum and lymphopathia venereum, 322
Gridding the femoral head and neck area in fracture of neck of femur, 237

Head injuries, 232
Heart, contusions of, with aortic regurgitation; complete recovery, 110
Hemorrhagic purpura; splenectomy in treatment of, 340
Hernia; difficulties and dangers of injection treatment of, 300
epigastric, 376
huge ventral, complicated by incarceration of gangrenous ileum, 107
intra-abdominal, 374
left intraperitoneal, 104
modified operation for correction of inguinal, 306
Hirschsprung's disease (megacolon): treatment by one-stage extraperitoneal resection, 272
Huge ventral hernia complicated by incarceration of gangrenous ileum, 107
Hyperinsulinism, 241

Inexpensive skeletal traction apparatus, 395
Inhalation analgesics in obstetrics, 463
anesthesia; carbon dioxide absorption method in, 456
present status in, 446
anesthetics; pharmacological action of, 435
Injection treatment of hernia, difficulties and dangers, 300
Injuries, head, 232
Intestinal obstruction, 72
Intestine, small, and appendix; argentaffin cell tumors: "carcinoids" of, 294
volvulus of, 286
Intra-abdominal hernia, 374
Intravenous anesthesia, 559

Jaundice associated with toxic goiter, 338
Jejunal diverticulosis, 369

Kidney; surgical treatment of transcapsular rupture of, 76

Labor; observations and aids in rectal and vaginal examinations during, 65
Large vesical calculus, 94
Left intraperitoneal hernia, 104
Lithotripsy, clinical and experimental study of, 34
Liver extract, effect of oral and parenteral, on hematopoiesis in splenectomized dogs, 248
function; anesthetics and, 486
Lobectomy for central abscess of lobe; hinge flap for multiple bronchopleural fistulas; post-tonsillectomy peripheral lung abscess, 83
Local anesthetics; applied pharmacology of, 500
Lung abscess; lobectomy for central abscess of lobe; hinge flap for multiple bronchopleural fistulas; post-tonsillectomy peripheral, 83
Luxatio testis traumatica, 18
Lymphogranuloma; anorectal syndrome of, 316
Lymphopathia venereum and granuloma venereum, 322

Madelung-like deformity, unusual type of, 365
Malignant tumor of Meckel's diverticulum, 101
Medication, preanesthetic, 428
Megacolon (Hirschsprung's disease): treatment by one-stage extraperitoneal resection, 272
Mercresin, a new surgical germicide, 47
Modified operation for correction of inguinal hernia, 306
Morphine as an aid in diagnosing acute abdominal affections, 5
Mortality of spinal analgesia, 606
Mucocele of appendix, 383
Mudd, Dr. Samuel A., hero of the Dry Tortugas (Bo.B.), 397
Muscular spasms during general anesthesia; etiology of, 474
Myositis ossificans, 227

Neck; regional anesthesia for operations on the, 531
New apparatus for reduction of tibia and fibula, 396
Nephroptosis, 41
Nephroureterectomy, a new technique of, 206
Neurofibromatosis of bladder and prostate, 90
New instruments in plastic operations on renal pelvis and ureter, 125
method of indirect blood transfusion, 119

Observations and aids in rectal and vaginal examinations during labor, 65
on the use of tribromethanol (avertin), 598
Obstetrics; inhalation analgesics in, 463
Obstruction, intestinal, 72
two quantitative tests of peripheral vascular, 71
Osteosclerosis (traumatic) of carpal bones, 357

Perforation of gall bladder; early gangrene of common duct, 97
Peripheral vascular obstruction; two quantitative tests of, 71
Peritoneal immunization, 266
Pharmacological action of inhalation anesthetics, 435
Pharmacology, applied, of local anesthetics, 500
Picrotoxin; the protective action of, in prolonged surgical anesthesia with evipal, 571

Plastic operations on renal pelvis and ureter; new instruments in, 125
Postoperative anuria, 352
Preanesthetic medication, 428
Preoperative estimation of the anesthetic and surgical risk, 410
Present status of inhalation anesthesia, 446
Proctological problems of the general practitioner, 309
Proctology; evipal anesthesia: its use in, 581
Progress of anesthesia (E.), 405
Prostate gland, abscesses of, 348
  neurofibromatosis of bladder and, 90
Prostatic obstruction, changing conceptions for indications for surgical relief of, 216
Purpura; splenectomy in treatment of hemorrhagic, 340

Recognition of anesthesia as a specialty (E.), 409
Rectal carcinoma, critical analysis of methods of treatment of, particularly electrocoagulation, 57
Reduction of tibia and fibula; new apparatus for, 396
Regional anesthetics: agents and methods, 511
  anesthesia for operations on the neck, 531
Renal pelvis and ureter; new instruments in plastic operations on, 125
Respiration; a new apparatus for artificial, 611
Resuscitation, 591

Short history of stomach surgery (Bo.B.), 127
Simplified method of drawing blood for citrate blood transfusion, 620
Soul; an inquiry into several beliefs held by men regarding the anatomical site of the, (Bo.B.), 621
Spasms; etiology of muscular, during general anesthesia, 474
Spinal analgesia, mortality of, 606
  anesthesia, 519
    a special syringe for use in, 615
Splenectomy in treatment of hemorrhagic purpura, 340
Stomach surgery; short history of, (Bo.B.), 127
Surgery; anesthesia and (E.), 408
  present trend in, (E.), 1
Surgical treatment of transcapsular rupture of kidney, 76
Survey of breast cancer incidence in New England, 331
Syringe, special, for use in spinal anesthesia, 615

Testis, luxatio, traumatica, 18
The effect of oral and parenteral liver extract on hematopoiesis in splenectomized dogs, 248
  present trend in surgery (E.), 1
  protective action of picrotoxin in prolonged surgical anesthesia with evipal, 571
Thyroid crisis complicating surgery, 391
  enucleation of superior pole of, 201
  gland, diseases of, 12
Traction apparatus, inexpensive skeletal, 395
Transfusion; new method of indirect blood, 119
  simplified method of drawing blood for citrate blood, 620
Transsacral and caudal block, 539
Transurethral resection of bladder tumors, 113
Treatment of acute empyema, 50
Tribromethanol (avertin), observations on the use of, 598
Tuberculosis of appendix, 379
Tumor, malignant, of Meckel's diverticulum, 101
Tumors, "argentaffin" cell: "carcinoids" of small intestine and appendix, 294
  transurethral resection of bladder, 113
Two quantitative tests of peripheral vascular obstruction, 71

Umbilical cancer, 116
Unusual type of Madelung-like deformity, 365
Ureter, diverticulum of, 387

Vascular obstruction; two quantitative tests of peripheral, 71
Ventral position for drainage in ruptured appendicitis, 69
Ventricular fibrillation in anesthesia, 496
Volvulus of small intestine, 286